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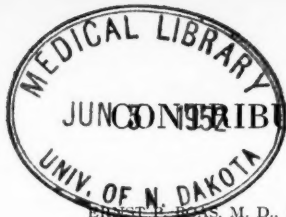
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CLINIC OF DR. NELLIS B. FOSTER

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FUNCTIONAL DISORDERS SIMULATING ORGANIC DISEASE

IN ancient medicine some emotional disorders and perversions of inhibition were ascribed to uterine disease. The only vestige of this idea now remaining is the name—hysteria. But it was not many years ago that a whole array of psychoneurotic symptoms were assigned to ovarian disease, and ovaries were quite enthusiastically removed until a thoughtful surgeon called attention to the apparently normal condition of many of these organs, and expressed the belief that every surgeon who performed ovariectomy should be forced to show cause for it. Other examples of supposed organic disease and various methods of treatment come to mind—theories and enthusiasts that flourish for a day, then pass and leave no mark. Despite the testimony of mountains of crutches at Lourdes and at St. Anne de Beaupre, and healings through the ages by every sort of occult means, yet one of the most difficult concepts for the medical mind to grasp—by the laity never grasped—is the idea that abnormal functional behavior may arise without organic disease as a cause.

Neurologists are in the habit of speaking quite casually of functional disorders, but is it so definite that a disorder in function can arise in a healthy organism? Is there not always the tacit reservation that the organism is healthy only in the sense that by methods now available no disease can be detected? We have current notions that express something, yet do not bear

philosophic analysis; such terms as "functional disorders lead to organic disease." Just how can this occur? Even the intangible emotional upsets which induce chemical and physical changes in body fluids are themselves probably resolvable into chemical and physical interpretations. I only wish to call your attention to this aspect of medicine which is now limited to speculation, but it should prevent us from falling into pitfalls of dogmatic theory and system which have always hindered the growth of knowledge. We can keep an open mind about the causation of neuroses and still recognize that their protean syndromes may simulate definite organic diseases.

Nervousness, tremor, and tachycardia are symptoms which occur in several psychoneurotic disorders. When these symptoms are associated with an enlargement of thyroid the clinical picture resembles closely that of thyrotoxicoses. A number of cases have come to my attention each year because they have not been benefited by operations on the thyroid. Sometimes they are injured by the operation, since the effect of operations on psychoneuroses is apt to be harmful. To illustrate how closely the picture of Graves' syndrome may be simulated by purely emotional upsets, consider this case. A girl of eighteen was referred as a case of Graves' syndrome. The facts on which this diagnosis was based were goiter, tremor, and tachycardia. The patient stated that she had been well until an accident last summer. While boating she was capsized and badly frightened. At once after this she had experienced palpitation, which had persisted. She had also been nervous, had slept badly, and felt anxious and irritable. She believed that her neck had become fuller. There was a small but definite goiter, a tremor, and tachycardia. The eyes were prominent, but not to a degree to be called exophthalmos. The tachycardia, it was found, was variable and disappeared during sleep, and vanished entirely after a couple of days of reassurance. Basal metabolism estimations were done several times, with constantly normal results. My interpretation of the facts in this case are that an emotional young woman with adolescent goiter met with an accident which gave rise to an anxiety neurosis. Had she been treated as a case

of thyrotoxicosis the neurosis might have become fixed for life. Small doses of iodine for the adolescent goiter and liberal doses of psychotherapy combined with a healthy environment help these patients remarkably, but, judging from the cases I have seen after surgical treatment, operations are often a disaster. Moderate hypertrophy of the thyroid is not uncommon in young women; it requires a definite treatment, but when this goiter happens to develop in an individual with psychoneurotic symptoms the result is not Graves' syndrome, although the resemblance to it may be close indeed.

Fear is the strongest of primitive emotions, and anxiety neuroses, since they hold the fear element, are the most apt to produce clearly defined functional disorders. Fear (and hence anxiety) has its notable influence on heart rate and vascular tone, and also upon the several factors of digestion. To a less degree, but quite as definitely, other emotions may have the same result in disposed individuals. The effects of these emotions are expressed as vasomotor manifestations. Many of the symptoms of Graves' syndrome are vasomotor in origin; tachycardia, for example, hence a resemblance between different disorders arises.

Palpitation and tachycardia may be early evidences of serious cardiac disease, and probably for this reason they are sometimes given undue weight in formulating an opinion of an abnormal action of the heart. The stress given to the diagnosis of functional heart disorders during the war was of general benefit, but it still seems to require an undue amount of courage to decide that a young man may be sound even though he have tachycardia and a slight systolic blow in the apex region. The signs and symptoms of what we now call neurovascular asthenia—dyspnea, tachycardia, precordial pain, and palpitation—are one and all possible evidences of organic disease, but they are, on occasion, also evidences of a constitutional type or of poor physical tone. Differentiation depends on consideration of all the evidence—history of infections, habits of life, body conformation, the effect of exercise and rest on the heart's action, and muscle tone. The fact here to be impressed is that not only subjective

symptoms but physical signs as well can be misleading. And I do not think of any tragedy that may befall a healthy young man more serious in warping his future life than to tell him he has heart disease. It seems to leave a scar which no experience can effectually eradicate. In disorders of the heart especially it is the part of wisdom to give a prognosis on the best supposition, to treat the patient on the worst. And in the case of young persons particularly we should not hazard the diagnosis of organic heart disease except with the best of evidence at hand. A systolic murmur in the mitral region, alone and without known etiology, is not good evidence.

One of the commonest of human ailments is headache. Its causes are numerous, some known, many unknown. When there is no obvious cause and there is a sort of predisposition the disorder is termed "migraine." This term explains nothing, it does not even classify, but it too often satisfies. In some individuals there is a clear predisposition to headache, the most trivial episodes are adequate stimuli to provoke this response. Slight fatigue, even unusual excitement. These are, by common consent, highly organized persons of clearly neurotic types, but to say this is only to admit that in their cases slight causes produce results which would be produced in more stable organizations by heavier shocks. A brain tumor, or meningitis, or sinus infection will probably induce headache in anyone, but the results of study of migraine in the last few years suggests that the disorder is often traceable to a peculiar sort of hypersensitiveness, an unstable state of tissue colloids possibly. In some cases the reaction is produced by protein, in others by carbohydrates. The feature of interest to me is that these results, as far as they go, would seem to bring some cases of migraine into a larger general group which encompasses asthma and hay-fever. Now all of these diseases have been in the past regarded as neuroses; there is some common resemblance in the constitutional make-up of those predisposed to these diseases which has been often noted. Unless serology find a means there is, however, nothing in the grouping but an indefinite impression. There is no test to which all of these and none other

respond, but the commonness with which members of these groups develop some form of sensitization provokes speculation as to whether perhaps the immediate symptom in general may be a colloid reaction and the basic predisposition a physical state explicable one day in terms of colloid chemistry.

Of all the conditions wherein functional disorders resemble organic disease, the gastro-intestinal tract furnished the most numerous examples. The effects of love and grief are known to everyone. Anxiety and apprehension may produce symptoms and a degree of emaciation that suggest malignant disease. Profound disorder of digestion is comprehensible in the light of physiologic experiments, that emotional states can inhibit secretion and influence peristalsis.

A couple of years ago I analyzed about 3000 cases of gastro-intestinal disorders. The results of this analysis are interesting:

Organic disease:		
Neoplasms.....	84	Per cent.
Ulcers.....	305 =	389 14
Reflex disorders:		
Adhesions and appendicitis.....	522	
Gall-bladder.....	397	
Constipation.....	138	
Pelvic disease.....	48 =	1105 39
Systemic disease:		
Kidneys.....	154	
Cardiovascular.....	102	
Pulmonary.....	88	
Blood and ductless glands.....	53	
Organic nervous disease.....	30	
Infections.....	38 =	465 16
Functional disease:		
Neuroses.....	384	
Constitutional asthenia.....	71	
Achylia.....	123	
Migraine.....	42 =	620 22
Diagnosis undetermined.....	186	6

According to this analysis nearly one-fourth of the cases were of a functional type and gave no evidence of organic disease in the accepted meaning of that term, but in many instances the symptoms for which the patient sought relief were

as characteristic of organic disease as of functional disorder. The usual symptoms, in some combination, were: pain, nausea, vomiting, anorexia, flatulence, emaciation, and these are common in cases of ulcer and cholecystitis or neoplasm. It is not the object here to detail the methods of differentiation of functional from organic disease, but to call attention to a similarity which may prove an embarrassing pitfall. We have all made these errors in diagnosis, and lucky is the surgeon who has not operated on a psychoneurotic patient for supposed ulcer.

A CLINICAL LECTURE BY DR. HARLOW BROOKS

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CHRONIC GALL-BLADDER DISEASE AND CHRONIC APPENDICITIS

EVERY physician, be he surgeon or internist, must have been struck with the frequency with which patients come to him with the story that Dr. "So-and-So" tells me that I have gall-bladder disease, and Prof. "Somebody-else" tells me that I have a chronic appendicitis, now what do *you* think I have?

Of course, in case the man consulted was a surgeon, in either instance his advice has been Operate. The average patient, however, fails to enthuse over the project of operation under a questionable diagnosis. I can quite well understand his reticence, for if he has prefaced his consultations by talks with his friends and associates he will find abundant instances in which he will be truthfully told of operations for this or that condition without full relief of signs or symptoms, and even with completely negative findings. In many instances of this kind, in which I have spoken directly to my colleagues concerned, more often than not I have received from them the more accurate information that although they may have told the patient positively that he had a gall-bladder disease or an appendicitis, this certainty of opinion was not really the full conviction of the physician, but a positive answer was given because of the unhappiness which a qualified and uncertain diagnosis often brings to a patient, and also because he was in his own heart convinced that in either case the preferable treatment was the same, namely, an exploratory operation.

More than infrequently I have also had patients come for an opinion or for medical relief because of the persistence of signs

and symptoms after the operation, with the story that they were operated for either a chronic appendix or for a resection of the gall-bladder when the character of the scar fully indicates that the operation was really made as an exploratory, both conditions having been properly in the mind of the operating surgeon.

No one but the most enthusiastic of surgeons can expect 100 per cent. perfect results in either condition, and I am in no way criticizing in this remark, for I am certain that even the most positive of surgeons would quickly lose faith in surgical infallibility if he might stay for a few days in the consulting room of the average internist. Even in chronic appendicitis, correctly diagnosed and skilfully operated, by no means complete relief of long-standing symptoms and signs are to be always expected. Even more frequently is this the case in operations for gall-bladder disease.

Is all this the result of careless or of incorrect diagnostic methods? Certainly the experience of surgeons of very wide training negatives this probability, for the frequency with which chronic appendicitis and chronic gall-bladder disease are found associated is very great. Every pathologist knows also that even the most skilful surgeon may pass over a gall-bladder at the operating-table as entirely normal, when close postmortem examination may show extensive and long-standing disease of the mucosa or of the ducts. The almost universal practice of surgeons to always remove the appendix whether thought normal or abnormal eliminates errors of this character in so far as the appendix is concerned.

Just a sentence of explanation before we proceed further as to what we mean by chronic gall-bladder disease. The term in this clinical relation must be very widely applied for the reason that accurate differentiation between chronic cholecystitis, adhesions about the gall-bladder, sclerosis of the gall-bladder, and some cases of cholelithiasis is extremely difficult if not impossible on a symptomatic or gross pathologic basis. Chronic cholangitis also can by no means be always differentiated, and the pathologist finds it present in a considerable number of

cases of chronic inflammations of the gall-bladder in which it could not be clinically or surgically identified. Doubtless this accounts for a good many cases of gall-bladder resection in chronic disease most skilfully performed, but which fail to give relief from the symptoms present in the case.

Assuming as we must the frequency of the dual occurrence of chronic gall-bladder disease, and of chronic appendicitis, is this relationship a mere chance or coincidence? One can hardly presume this in the face of its frequency, and we must further accept that the association of the two lesions is more frequent than even the surgeon finds to be the case at the operating-table if we consider in this respect the findings of pathologic anatomists.

Is then the clinical confusion due to the admitted great difficulty of differential diagnosis? The actual finding of the commonly associated lesions shows the incorrectness of this assumption, and we must, at the best, further assume a considerable number of chronically diseased gall-bladders which escape recognition, in the presence of an active appendix when close investigation of the gall-bladder condition is impractical.

Does one lesion cause or invite the other? If so, which is the primary? The intimate relationship which exists between the two organs through their lymph and blood-supply suggests this possibility, and in this case one would expect the appendix to be the probable earliest focus. The etiologic pathology of appendicitis is still very vague and uncertain, and one can by no means assert positively that the chronic gall-bladder and the chronically inflamed appendix may not have a common source, as, perhaps, through some such specialized or specifically sensitized infection as Rosenow, of Rochester, has suggested.

Were it not that the actual and indisputable lesions are found associated in more than a chance percentage of occurrence, one might be quite justified in assuming that the clinical confusion in cases might be due to the very close similarity between the signs and symptoms of the two conditions. For this reason I shall, at the expense of considerable time, enter into the diagnosis of the two conditions especially because one certainly

cannot recommend that in every appendectomy the gall-bladder should be removed, though I think that except in emergency cases it should certainly be examined. Such a step might, of course, tremendously increase the mortality rate in appendectomy, and in many instances at least this added risk would be entirely unnecessary and unjustified. Several surgeons even go so far as to assert that the removal of a diseased appendix when associated with an infected gall-bladder goes far to improvement of the gall-bladder lesion in itself. I am inclined to agree with them.

Signs and Symptoms of Chronic Appendicitis.—I realize perfectly that in reviewing this familiar picture I shall be accused, and perhaps justly, of wasting your time, but I shall try to detail these signs and symptoms from the standpoint of differential diagnosis, and as I have seen them, rather than from the text-book basis.

First, as to the chief symptoms which occur in chronic appendicitis. They may be practically all comprised under the heading of gastro-intestinal disorders. Colonic and gastric inflation with gas, with or without eructations. Distress, dull pain and gastric sense of weight after eating, a constipation which is often made worse in so far as symptoms of gastro-intestinal disturbances are concerned by the giving of purgatives, but in which relief of a more permanent character may follow colonic lavage. Actual pain may be complained of in the classic region of the appendix, or none whatever may be present. Occasionally this pain may be reflected into the back or down through the ring along the spermatic cord. As a rule, careful investigation of the history of the case will elicit a story of acute attacks of probably appendicitis far back in the history, and almost inevitably one of recurrent attacks of the symptoms which have just been mentioned. These attacks will be noted to occur most frequently when dietetic indiscretions have been committed, but they may also develop spontaneously as it were out of a clear sky, or after exercise, especially such as involves the lower abdominal muscles. More often than otherwise progressive loss of weight will be found to have taken place, and

though the patient will state that a meager diet, as a rule, gives less disturbance, dietetic restriction will not, however, even when most carefully supervised both qualitatively and quantitatively, entirely prevent the ultimate development of attacks. The patient will also occasionally note that certain particular forms of exercise, such as jumping, long climbs, or horseback riding, will induce attacks.

Pain may be located high up in the abdomen, occasionally in the median line, or on the left side of the abdomen far from the customary or actual location of the text-book appendix. Frequent nausea and even vomiting may occasionally occur. Tenderness is often not constantly present, but it is almost always occasionally, and with it still more constantly rigidity, which, however, is in chronic cases rarely as sharply located as in the acute disease. Quite as frequently as not it is most intense, with a corresponding rigidity in the upper quadrants of the abdomen, and very commonly deep pressure over the hepatic flexure of the colon, that is, near the location of the normal gall-bladder, causes local tenderness or even reflected tenderness in the right lower abdominal quadrant. Sometimes the rigidity of the abdomen involves the whole right side, and pain on deep pressure may be referred to the back in the region of the right kidney. Biers' sign may be present. Of course, in a good many cases a definite tumor mass may be palpable in the classic McBurney's point with tenderness, and the usual local groups of symptoms and signs. In a good many cases careful rectal examination will show rigidity and occasionally mass. As a rule, one is most successful in rectal examination when the patient is turned on the right side.

x-Ray examination in my experience has been very unsatisfactory in so far as absolute diagnosis of chronic appendicitis is concerned either in a positive or negative way. Some radiographers assert that an appendix which fills and retains the opaque material after the colon has largely emptied indicates chronic inflammatory change, others state exactly the opposite. Abnormal positions of the appendix may, however, be often well visualized, and adhesions are shown or suggested in the average

number of cases. What is at times particularly confusing is, however, duodenal spasm or apparent stricture, evidently caused reflexly by the appendical process, and which may fail to be apparent on laparotomy. In several instances of this kind excellent radiographers have positively asserted that duodenal defects, stricture, or adhesions were present in these cases of chronic appendix, and yet none could be found at subsequent operation or autopsy. More than occasionally gall-bladder disease has been suggested by the roentgenologist from his findings alone, and yet at operation only appendical disease is discovered. Of course, in a preponderating number of such instances, associated gall-bladder disease was also present. It is well to know that x-ray findings may absolutely mislead in diagnosis quite as much as physical signs and symptoms.

Aside from x-ray work little in the way of laboratory findings is of material help in the direct diagnosis of chronic appendicitis, except, of course, in those instances in which an active inflammatory process supervenes, when, of course, leukocytosis and physical tumor with definitely localized tenderness and pain are to be expected.

Chronic gall-bladder disease presents, as you will see in a large group of cases, a series of symptoms and signs very similar in many to those which have just been detailed. Please understand that I am not now describing the typical text-book picture of chronic gall-bladder disease, nor am I drawing from the literature as much as from my own experience in the consulting room.

History is usually much less definite and helpful in the gall-bladder cases. One may get a definite story of a previous attack, or even of recurrent attacks of jaundice, associated with gastro-intestinal disturbances, such as, for example, might have appeared in acute catarrhal jaundice. More or less cramp-like pains may have taken place, as in gall-stone attacks, but usually the story is one of persistent recurrent attacks of nausea, perhaps with vomiting, "gas on the stomach," bloating of the abdomen, loss of weight, constipation often alternating with diarrhea, great difficulty in the choosing of foods which are tolerated with

relative comfort, perhaps occasional slight jaundice, tenderness, and pain in the upper abdomen and epigastrium, often reflected downward into the right lower quadrant especially. Jaundice is a much less frequent sign than is generally assumed, and is ordinarily only present when obstruction of the common duct is present. It is quite as frequent in instances of inspissated bile as in gall-stones. Tight clothing has become uncomfortable and attacks of "water-brash" are frequent. The urine at times may contain small traces of bile, even though no real icterus may be present. A more or less progressive secondary anemia may appear and the patient finds himself losing both strength and weight. Mental depression is the rule, particularly as he finds that treatment is rather unsatisfactory in so far as giving relief is concerned, while a very abstemious and careful diet must be maintained. Cardiac distress or actual myocardial disease may appear.

Occasionally evidences of pancreatic disease appear, and especially in older patients an occasional trace of sugar may appear in the urine. Occasionally slight elevations of temperature may occur from time to time, though, especially with the presence of jaundice, a subnormal pulse and temperature may be present. Ordinarily no changes in the blood-count are present except when an active and usually unmistakable cholecystitis appears. Cardiac arrhythmia and a lowering of cardiac muscle reserve may become evident.

Physical examination will usually present as its most striking finding rigidity in the right upper quadrant, though the whole side may be stiff and tender on percussion or firm palpation. By no means infrequently it will be found that pressure in the usual location of the gall-bladder will cause definite pain in the right lower abdominal quadrant, though one may find at operation or autopsy no actual appendical disease present.

Occasionally definite sharply located tenderness over the gall-bladder is made out, and this sign will ordinarily be found to vary greatly from day to day, so much so that one is very chary about making an absolute diagnosis on a single examination. Sometimes a line of definite tenderness is found in the

epigastrium, leading from right to left, usually extending with a diminishing degree of tenderness. Sometimes the entire liver is tender and sensitive on firm pressure or heavy percussion. Emaciation may be of such character that a suspicion of hepatic neoplasm arises. As a general rule it will be found in these doubtful cases that the location and degree of rigidity of the abdomen varies very much, and at times a definite tumor mass may appear to be placed in the customary region of the gall-bladder and at other times it is certainly absent. Not at all infrequently deep pressure over McBurney's point will cause acute pain to appear in the region of the gall-bladder, and at times both at the point of pressure and in the gall-bladder region also.

x-Ray study is sometimes very helpful and sometimes very disconcerting in these cases. Of course, in fortunate instances a definite gall-stone may be shown, even in patients in which the clinical findings on which to base such a diagnosis are very few, but more frequently the opposite is the case. Occasionally in cholecystitis a definite and very convincing gall-bladder shadow may be thrown, and also in cases in which one may be morally certain of the diagnosis nothing helpful in either direction may appear. Duodenal defects, as from pressure spasm or from adhesions, may be suggested, and these may vary so much at different times or in the hands of different technicians that one is forced to entirely discredit the findings in his conclusions or to consider the work as entirely negative, unless one is willing to accept only occasional positive findings.

How is one then to make an absolute diagnosis in these cases, especially when one realizes the great frequency with which the two conditions are associated? It is very easy indeed to say operate and find out, but it remains to convince the patient to submit to this step, especially since he should be fairly told that the diagnosis is not certain and that absolute relief cannot be promised.

Many patients because of accompanying conditions—a bad heart, a tuberculosis, or of some other complicating or concomitant state—are a poor operative risk. One cannot promise the

patient full relief or even partial relief from his symptoms, especially if the strong suspicion of associated gall-bladder and appendix is present. The double operation is by no means a trivial one, and even a satisfactory exploration may not be by any means a simple matter. If one operates under the diagnosis given to the patient of a simple chronic appendicitis, and fails to give relief or benefit, he brings surgery into disrepute at the patient's expense, and without benefit to anyone. The number of such cases which come ultimately to the internist is large, and they are a difficult and suspicious type of patient from every standpoint. It has been my growing conviction that the patient should be fully informed of the question in his case and that he should at least share the responsibility of exploratory or medical treatment. One may in suitable cases make the probable diagnosis of chronic appendix, at the same time stating to the patient that the possibility or probability of gall-bladder disease also exists, requesting permission to make the exploration after the appendectomy has been performed, and to then do what seems indicated in the best judgment of the surgeon and of the family attendant, if he be present, as he should be at the operation.

It may seem wise to do the appendectomy alone, and where no gross disease of the gall-bladder is evident, to close the abdomen in the hope that all symptoms may have originated from the appendix, or that, if associated gall-bladder disease was present, the appendectomy may also relieve it, as I am convinced sometimes occurs.

Postoperative medical treatment is necessary in nearly all of these cases, even those in which apparently the lesion was a single one or in which complete operative correction has been permitted and accomplished. Perhaps there is something of a habit in disease symptoms and signs, at least we all of us see cases in which symptoms persist even though the causative lesions have been removed. This has, in my experience, much more frequently followed those cases in which the dominant disease seems to be of the gall-bladder rather than of the appendix, and in this respect I believe that I voice quite generally

the experience of most internists in so far as postoperative gall-bladder cases are concerned.

What then may be done for the case which refuses operation, in which operation is not advisable because of other disease, or in which, after operation, is not attended with sufficient degree of relief?

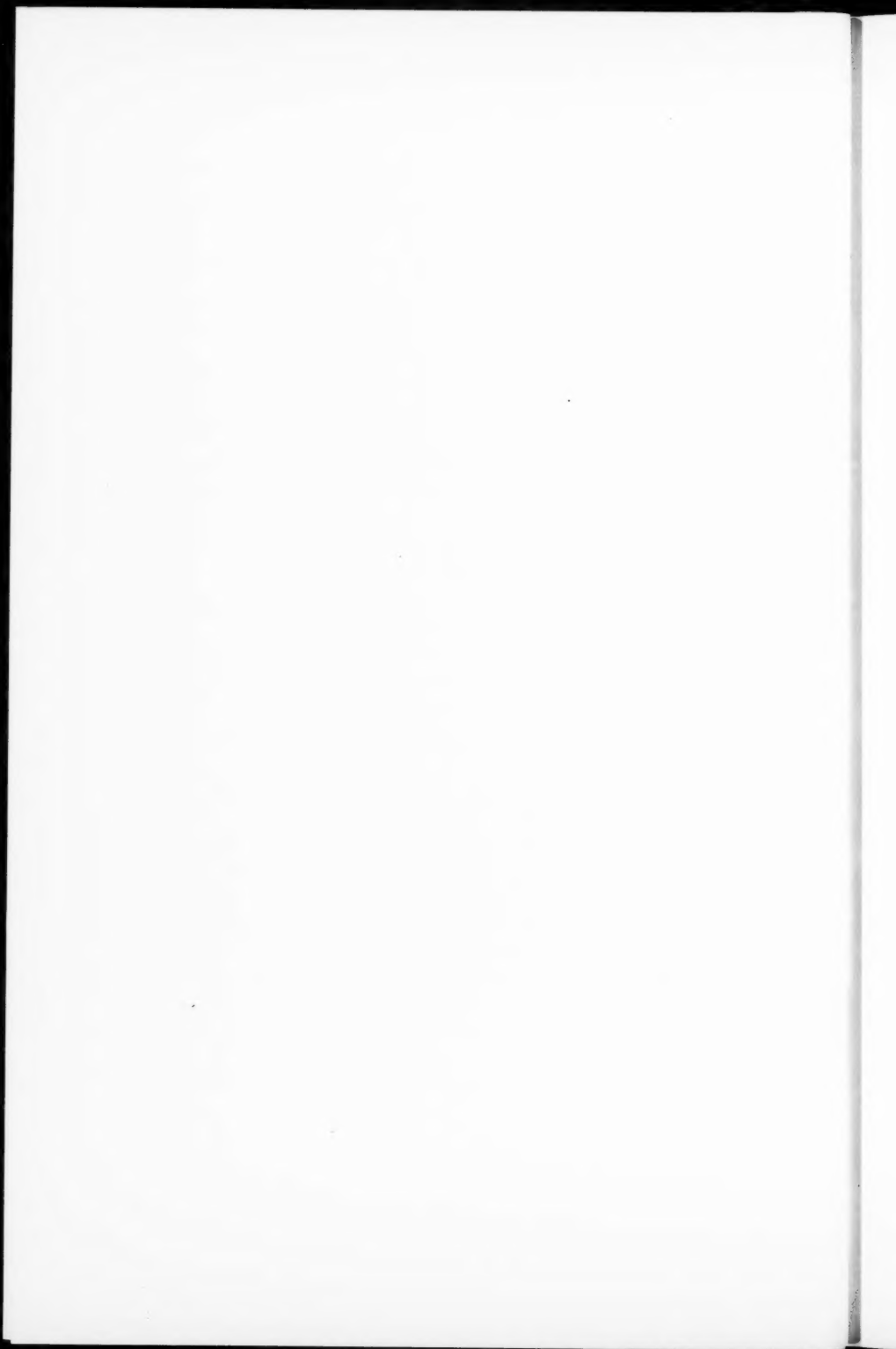
Diet is of paramount importance. It must be small in amount, usually no more calories than the occupation of the patient demands for his maintenance, and it must be notably small in bulk, even though constipation exist. Roughage foods are, as a rule, very poorly tolerated. Experiment only can show what foods are most acceptable in any individual case, but in general I have found best results from a start with substantially the sort of diet which is employed in gastric hyperacidity. Unless the liver tissue is itself involved, I have found no adverse results to follow the use of the usual meats, though, of course, more than ordinary care is necessary in the preparation of the foods. Highly spiced, fat, acid, and sweet foods are usually to be barred. Milk is often poorly tolerated, but should be used otherwise.

The alkalies frequently give tremendous symptomatic relief; sodium bicarbonate forms the usual basis of these, but one adds magnesium salts, especially the heavy oxid or magnesium *ustæ*, as needed to correct the constipation if it exists. Bismuth salts may be used also as indicated. The alkalies are best administered thirty to forty minutes after feeding, and when it has been found best to give foods in frequent small quantities the doses of the alkali may be proportionately decreased.

Where the bowels are not easily corrected by the alkalies, one may advantageously use high colonic irrigations, preferably with alkaline solutions, but if these are too persistently utilized I am convinced that serious disease of the colon sometimes develops from it.

The Meltzer-Lyon method of use of magnesium acts very well in some cases, and I have seen apparently excellent results in the hands of physicians expert with this method of treatment, though in some instances it has not alone failed to benefit, but has made the patient apparently worse.

At best the treatment of these cases is unsatisfactory, and the only brilliant results follow successful surgery, but with so small a percentage of 100 per cent. results that one does not feel like urging operation, but throughout the medical management of any case, even after operation in the hands of very skilled surgeons, the internists must remember that at any time surgery may again become indicated.



CLINIC OF DR. WALTER L. NILES

BELLEVUE HOSPITAL

CONGENITAL FIXATION OF THE DUODENUM BY HEPATODUODENAL MEMBRANES (HARRIS BANDS)

APPRECIATION of the frequency and importance of disturbances of the duodenum is so recent that, with the exception of ulcer, little is as yet to be found in the text-books concerning them.

I propose today to show you several patients who illustrate one common type of duodenal disease, viz., congenital fixation by anomalous membranes.

Case I.—This white female patient is thirty-four years of age and a secretary by occupation. She has never had any serious infection. Menstruation began at fifteen, is always regular, rather scanty, and never painful.

From the age of thirteen months to four years she had many convulsions. In her twenty-second year she had two attacks which were said to be convulsions; she has had none since. She has never had bilious attacks, headaches, nausea or vomiting, although she has always been constipated.

One day about seven years ago she went to business feeling perfectly well. About two hours after luncheon she began to have pain in the pit of her stomach. This was quite severe and was also felt under the manubrium. Her epigastrium was distended and she belched large quantities of gas, with temporary relief. There was no nausea or vomiting. The pain continued until the next morning. Since that time she has had many similar attacks at intervals of from three to seven weeks. They vary somewhat in severity, but have never required morphin, and are usually relieved by an enema or colon irrigation.

In January, 1921 the appendix and a part of one ovary were removed. Since this operation, however, the pain has increased in severity and is present practically all of the time, especially at night. She has recently been dieting, but thinks that the quality and quantity of food has little effect upon the pain. She constantly has considerable gas, which she belches. Her tonsils were removed in June, 1923. She has lost little if any weight and sleeps well if not disturbed by the pain in her stomach.

The patient is a fairly large, well-developed, well-nourished woman, distinctly pallid, and not at all nervous. Her physical examination is negative

except the abdomen, which is somewhat distended and shows a firm median scar running from the umbilicus to the symphysis pubis. There is distinct tenderness in the right lower quadrant, especially the upper portion. There is no tenderness in the gall-bladder region, but just to the right of the mid-epigastrium there is moderate tenderness. Percussion shows increased tympany over the cecum and ascending colon. No mass is felt, neither are the solid viscera palpable. Except for slight secondary anemia the findings of the clinical laboratory are negative.

Fluoroscopic and x-ray examinations show a fish-hook type of stomach with the lower pole crossing the spine at the level of the sacrum, while the apex of the duodenum is held at the level of the second lumbar vertebra. This, you will notice, is an unusually long ascending part of the stomach. The apex of the duodenum is definitely fixed at the point indicated, and the ascending limb together with the pylorus is pulled over to the right. The duodenum is sharply kinked, but there is no other deformity or filling defect. The stomach empties in four hours. There is moderate stasis in the colon and a redundant loop is seen in the sigmoid.

The x-ray evidence of anomalous fixation of the apex of the duodenum is perfectly definite, and this, together with the history, makes the diagnosis quite certain. I have advised operation, which will be done within a few days, and I have no doubt that the patient will be entirely relieved of her distress.

Case II.—This patient is an engineer, forty-two years old, and has lived an active, out-of-door life. He has suffered no serious infections and, although he has always had a tendency to constipation, he was fairly well, except for headaches, until the onset of his present trouble, which seems to have begun twenty-two years ago. In 1902 he suddenly developed a violent pain in the epigastrium which lasted for one day. He vomited several times. The pain did not radiate and there was no fever or jaundice. In two days he felt perfectly well. During the next nine years he had one or two similar attacks annually, which were relieved by taking castor oil. Since 1911 the character of the attacks has changed somewhat, but they have become more frequent. Every week or two he becomes uncomfortable in his lower abdomen and feels "rotten and draggy" all over. He has large quantities of gas in his bowels, loses his appetite, and feels distended. This may pass off in three or four days or, which is more usual, a steady, sharp pain develops in the epigastrium. He belches gas and is unable to sleep because of the pain. After a certain time the attacks appear to be relieved by a cathartic. In the intervals he feels quite well, but has some heaviness in his stomach, especially after large meals, and tends to constipation, though it is easily relieved.

In 1920, after a careful gastro-intestinal study which failed to reveal any definite condition, an exploratory laparotomy was performed. The incision was a low median and the surgeon failed to find any pathology except the appendix, which is reported to have showed a chronic obliterative process, and was removed. The patient made a good recovery, but within six months all of his previous symptoms returned.

Physical examination shows a well-developed, but somewhat pallid man.

He appears to be essentially normal except that his abdomen is somewhat distended with gas and there is well-defined, though moderate, tenderness in the right side of the epigastrium.

x-Ray and fluoroscopic examination shows a fish-hook type of stomach, which emptied in three hours. There are no indications of ulcer or malignant disease in the stomach or duodenum. The first portion of the duodenum is normal, but with the patient lying in the oblique position the first part of the descending limb seems compressed and runs horizontally for a short distance, then makes a sharp angle downward. It is firmly fixed in this position and contour. There are no other abnormalities in the gastro-intestinal tract and the urinary tract is negative.

The diagnosis of deformity and fixation of the duodenum by anomalous membranes is, in this instance, quite certain, for all of the common causes of abdominal pain have been eliminated by the previous laparotomy. It is probable that had the roentgenologist who made the study in 1920 been familiar with this condition of the duodenum, it would have then been recognized, or at least suspected, and the surgeon would have made an upper abdominal incision which would have easily revealed the cause of the symptoms. It is certainly difficult and, I think, usually impossible to recognize the condition by palpation alone. This patient has maintained his nutrition and stability of his nervous system better than most similar cases do, but he feels half-sick so much of the time that he is anxious for another operation, and I have advised it, as I believe that he will be entirely cured by simply mobilizing his duodenum.

I will now show you 2 patients who have been operated upon, so that you may form your own judgment regarding the benefits to be derived from such a procedure in properly selected cases.

Case III.—This man, now thirty-four years old, was operated on December 5, 1917. He gave a history of frequent vomiting and occasional diarrhea since childhood. If he became unduly fatigued or nervously upset, and frequently after ordinary exercise, he would vomit. He has always been subject to headache and bilious attacks. Attacks of pain, though never very severe, in his epigastrium have been frequent throughout his life. Six months before operation he had severe epigastric pain which lasted two hours and was relieved by vomiting. He had more recently become subject to cramping pains in his lower abdomen which were followed by diarrhea. He had suffered with "nervous indigestion" since childhood. This was described as a sensation of weight or heaviness after meals, especially after large meals. He belched gas, with relief, and sometimes his epigastrium became distended. Occasionally there was a dull pain in the epigastrium, but it seldom kept him awake, and was relieved by belching gas, for which he took bicarbonate of soda. His bowels tended to constipation except for attacks of diarrhea more recently. Eight months before coming under observation he had a "nervous breakdown" characterized by fatigability, mental depression, crying, and

indigestion. After three months of rest he improved and subsequently went to a military training camp. After one month all of his symptoms returned, and since that time he had been able to do little work. He slept well, but did not feel rested in the morning. His habits were excellent. His weight was 15 pounds under his previous best weight.

Physical examination showed a nervous, flabby, pallid young man, evidently poorly nourished. He gave every evidence of vasomotor instability and his reflexes were very active. Otherwise examination was negative except for his abdomen. This was boggy, slightly distended, and there was well-defined tenderness beginning in the right side of the epigastrium and extending to the right and downward to the right iliac fossa. There was no mass or muscle spasm.

Fluoroscopic and x-ray examination showed distinct indications of high duodenal fixation and some dilation of the cecum, which could not be dislodged from a position deep in the pelvis.

Operation showed that the duodenum was firmly held up close against the cystic end of the gall-bladder for about 4 cm., allowing displacement of less than 1 cm., by a membranous attachment which distinctly kinked and obviously caused partial obstruction of the duodenum. The fold of membrane was divided, which allowed the duodenum to move downward about 5 cm. and assume a normal contour. Exposure of the ascending colon and cecum revealed a well-developed Jackson's membrane which ran transversely across the middle of the ascending colon and caused constriction. There were no adhesions about the cecum or the appendix, which appeared to be normal, but was removed.

The patient made an excellent recovery. Within three months after his operation he enlisted in the Navy and served through the remainder of the war. He has since led a very active life and been perfectly well. He has no indigestion and weighs 40 pounds more than when operated.

Case IV.—This married woman, now aged twenty-nine years, first came under my observation on December 24, 1919, and was operated on April 6, 1920.

According to her history she had always had more or less indigestion. During childhood she had unexplained fevers and has always suffered with headaches. At eleven years her appendix was removed, it was said, for chronic appendicitis. She had then had 2 children, and throughout her pregnancies she had felt sick and faint and became anemic. The indigestion was described as a discomfort in the epigastrium coming on after meals, worse if she ate heartily or indiscreetly. It was not pain, but felt like the pressure of gas. With this she would become dizzy and nauseated and often had headache. The distress was relieved by belching gas or vomiting and occasionally by an enema. She was not at all nervous. Her weight was unchanged. She felt that the indigestion was gradually getting worse.

After a study of her gastro-intestinal tract a diagnosis of duodenal fixation was made and operation advised, which was, however, declined at that time. Despite careful treatment her condition progressed, and in February, 1920 she became so persistently uncomfortable and weak that she

was put in bed and placed on a modified ulcer treatment. She lost 15 pounds of weight and developed a moderate anemia. Operation was finally accepted and done in April, 1920. A thorough exploration of the abdomen revealed only a very thin adhesion between the cecum and the appendix scar, and a broad fold of peritoneum which passed from the back of the gall-bladder to the transverse mesocolon, surrounding and holding the duodenum high up and to the right of its normal position. This was divided, which allowed normal mobility of the duodenum. Her recovery was rapid and complete. She has since given birth to another child, and during the pregnancy felt unusually well. She has no indigestion whatever and regards herself as perfectly well.

These patients illustrate a condition which I have come to regard as one of the most frequent causes of indigestion. It is commonly overlooked by both roentgenologists and surgeons, for unless one is familiar with it and makes examinations for the purpose of detecting it or ruling it out, it is likely to escape notice. Careful fluoroscopic study almost always establishes the diagnosis, and it is the method of choice. Although x-ray films are aids and, of course, help in excluding other conditions, a combination of both methods offers advantages over either one alone.

Upon x-ray examination one usually finds a fish-hook type of stomach, often with a distinctly prognathian contour of the pyloric end of the greater curvature. The pylorus is found distinctly more to the right than normal and very high, often at the level of the first or second lumbar vertebra. The duodenal cap usually fills slowly because of spasm and is often larger than normal. The first portion of the duodenum is frequently dilated. The so-called hepatic flexure of the duodenum at the junction of the second and third portions is found very high, lying close to the liver and sometimes flattened by it. It is definitely fixed, shows no lateral mobility, and no up-and-down movement except with respiration. Quite frequently the duodenum gives the appearance of a soft tube suspended on a hook which, indeed, is practically its condition. Delay in the passage of the opaque meal at the point of angulation is often seen, but after a few minutes it passes on in a normal manner. While there is always some obstruction at the point of fixation, it is relatively slight compared with the resulting symptoms. Dilation of the

stomach is rare, and it usually empties on time. The tone of the peristaltic waves is good and sometimes there is hypermotility.

I have recently reviewed 35 cases which have been operated upon, and find that 29 were females and 6 were males. The largest number was in the third decade, but in most of them the symptoms began in the latter part of the second decade or the early part of the third. The youngest patient was aged fifteen years, while the oldest was sixty-seven years, and this patient's symptoms began only four years previous to operation. In general, it may be said that the older the patient, the longer the complaint of symptoms.

If symptoms have been present for many years the general picture is that which we recognize as neurasthenia. Chief among these manifestations are fatigability, nervousness, palpitation, tachycardia sometimes, headache often, and occasionally migraine, insomnia, and mental depression. These symptoms frequently overshadow the digestive picture.

The gastro-intestinal symptoms may be described as follows: from one-half to two hours after meals a sensation of weight or fulness or oppression is felt in the epigastrium. This is usually referred to as gas, and if belching can be induced some relief follows. Many patients take soda for this purpose and some find relief from an enema. Headache, nausea, nervousness, and depression often accompany the gastric distress. There is no distress when the stomach is empty, and those who take light breakfasts often have no discomfort until after lunch. Large meals, as a rule, cause more distress. Most of the patients had actual pain at some time, and some of them had severe pain repeatedly, but it is never agonizing, and an opiate is seldom required. Most of them vomited occasionally, especially after exertion or fatigue. Hematemesis or enterorrhagia were not noted. Heartburn and pyrosis occasionally occurred, but were not emphasized. There was little loss of weight in general, but several lost 10 to 20 pounds.

Constipation is the rule, and usually dates from childhood, increasing with successive years. This is sometimes varied by attacks of diarrhea and mucous colitis was noted in 6 cases.

There are no characteristic changes in the stools or gastric contents.

The results from operation are extremely satisfactory. Pain is always relieved, the digestion improves remarkably, and the general health, including the nervous state, improves correspondingly. The younger the patient, the more complete the recovery. The middle-aged neurasthenics respond slowly and seldom regain perfect health, but the improvement in some of them has been remarkable. Only one of the 35 cases which I have reviewed has not been very materially benefited, and she was an extremely neurasthenic middle-aged person who has been an invalid for twenty-five years. I think it is very important to recognize the condition in early age, and if it is pronounced to correct it at once, so that the individual may be spared subsequent years of semi-invalidism.

In closing I want to make it very clear to you that not all patients having congenital fixation of the duodenum require operation. In the majority of cases the fixation is relative or slight and the results of medical treatment are most satisfactory. Operation should be reserved for those who do not respond to treatment and those who relapse under the average conditions of useful lives. Medical treatment consists in giving a non-irritating, small residue diet in small quantities at frequent intervals, and administering antispasmodics and sedatives, of which belladonna or luminal are the most useful. Rest after meals and hot moist applications to the abdomen are also helpful.

Although anomalous membranes about the duodenum have long been recognized by pathologists and anatomists, it was not until 1914 that their significance and importance in causing distress and disability was brought to the attention of the medical profession by M. L. Harris, of Chicago. He reported 6 cases upon which he had operated, with satisfactory results, and very accurately described the origin of the pathology. Since then numerous reports of small groups of cases have appeared in the literature, but it continues to be overlooked chiefly, I think, because roentgenologists seldom make a sufficiently careful study

of the duodenum, especially beyond the first portion, when they only look for ulcer. Careful x-ray study almost always establishes the diagnosis with great certainty, although it is sometimes difficult to differentiate it from gall-bladder disease with adhesions, the condition for which it is most often mistaken.

Subsequent note: Case I was operated by Dr. Alfred S. Taylor on February 20, 1924, and his report follows:

The outer half of wound was filled by hepatic flexure, the inner half by pyloric antrum. The stomach came down well below the level of the umbilicus, but showed no intrinsic disease.

The duodenum was pulled far upward, backward, and inward by a membrane from the gall-bladder to the duodenum, the two organs being practically in contact through most of their length.

The apex of the duodenum was in direct contact with the cystic duct, the descending duodenum lying back of the gall-bladder, and this membrane was subject to considerable compression.

Also running from the fundus of the gall-bladder to the beginning transverse colon was a very firm fold of membrane which held the transverse colon high up against the gall-bladder and pyloric antrum and beginning duodenum.

The gall-bladder itself was apparently normal in size, texture, and color. The only abnormality was the very well-developed anomalous membrane, the attachments between the gall-bladder and the duodenum being so short that the two folds of membrane were considerably separated on the gall-bladder.

The dependent duodenum and the duodenojejunal angle were normal.

There were practically no adhesions to the inner surface of the old median scar. The only adhesions found were two small ones between the ends of two long fingers of omentum, one of which was attached apparently to the old appendix stump on the cecum and was about 3 mm. in diameter; and the other one was attached to the parietal peritoneum just to the outer side of the cecum.

The cecum itself was somewhat dilated, but was not adherent or held down by a pericolic membrane, but there was a well-developed, thickened, vascular pericolic membrane which crossed obliquely from below upward just above the cecum and caused marked kinking of the large intestine, as well as a knife-like compression where this edge of the membrane went across it.

There was marked thickening of the edge of the membrane so that a cord about 2 mm. in diameter was formed and caused most of the compression and disturbance.

Across the middle of the ascending colon was likewise another band which had developed in the pericolic membrane.

Also at the hepatic flexure was another fold which caused angulation and high fixation, this being in addition to the membrane coming from the gall-bladder down to the transverse colon.

Examination of the pelvic organs showed a somewhat infantile uterus

which was very markedly retroflexed. The cervix was large and hard, but the body between the cervix and the fundus was rather thin and quite flexible. The ovaries were both small and the right one somewhat cystic. There were no adhesions in the pelvis.

Palpation of the sigmoid could make out no abnormality beyond a very great redundancy, which was such that the sigmoid could be brought up into the wound.

The terminal ileum was normal.

Procedure: The hepato-duodeno-colic membrane was divided, the duodenum mobilized downward about 7 cm. and forward about 5 cm., so that it lay naturally below the fundus of the gall-bladder.

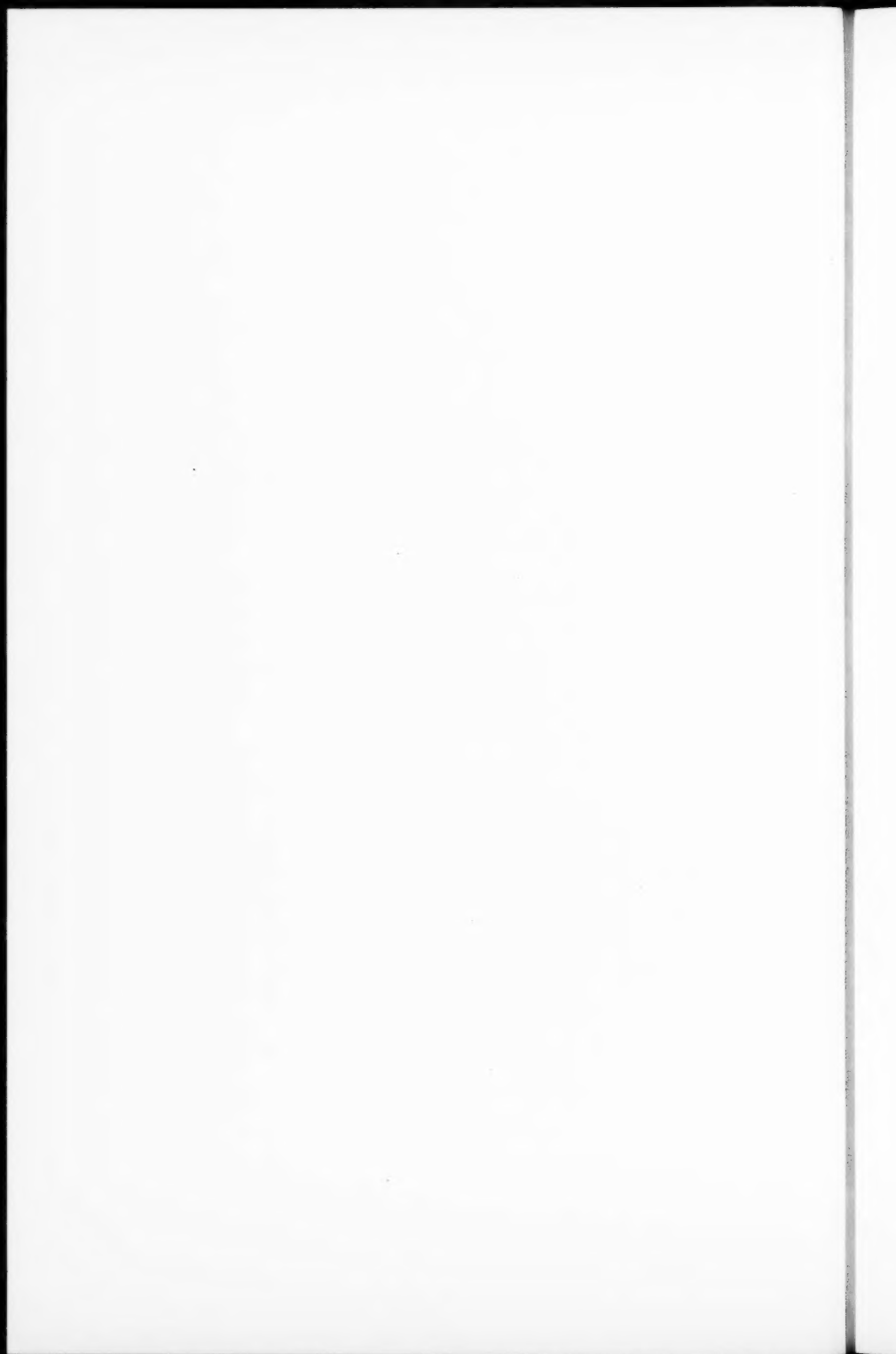
Also the transverse colon and the hepatic flexure were mobilized by division of the membranes, the upper border of the pericolic membrane being divided between double ligatures because of its vascularity.

The remainder of the pericolic membrane was divided downward along the outer aspect of the colon; and the two other bands described were divided between double ligatures.

The wound was closed by layer sutures and dressed as usual.

The patient is convalescing satisfactorily.

Case II was also operated by Dr. Taylor on March 16, 1924. A typical hepatoduodenal band was found, but no other important pathology. He is also convalescing satisfactorily.



CLINIC OF DRS. WILLIAM C. VONGLAHN AND
ALBERT R. LAMB

PRESBYTERIAN HOSPITAL

PRIMARY CARCINOMA OF THE LIVER¹

(CLINICAL PATHOLOGICAL CONFERENCE)

IN the past two and a half years at the Presbyterian Hospital we have had the opportunity of observing 4 cases belonging to a group which is of sufficient interest to justify us in bringing it to your attention.

As these cases present, in general, the same clinical picture and pathology, it will serve our purpose best, perhaps, to give you the case histories and the important postmortem findings first, and to discuss, finally, the essential features of the group as a whole.

Case I was a Chinese waiter of forty-seven years, who entered the hospital on November 12, 1921, and died three weeks later. He complained of persistently increasing swelling of the abdomen over a period of two months, with constipation, loss of weight and strength, and some pain across his chest, with a moderate cough.

He had been treated in this hospital four years previously for tuberculous glands of the neck and had had smallpox in his youth. Apart from these diseases he had always been well and had not used alcohol.

Physical examination showed a poorly nourished and developed Chinaman whose large bulging abdomen contrasted markedly with his wasted thorax and upper extremities. There was a small scar on the right side of his neck, and it was thought that he was very slightly jaundiced.

The rest of the examination was essentially negative with the exception of the abdomen. This was much enlarged and tense, with the overlying skin stretched and shiny. There was a definite fluid wave and shifting dullness. What appeared to be a hard nodular liver could be felt across the

¹From the Department of Pathology and the Department of Medicine of the College of Physicians and Surgeons of Columbia University, and the Presbyterian Hospital, New York City.

upper part of the abdomen, with masses in both flanks. The size and shape of these masses could not be made out on account of the large amount of fluid present. There was no tenderness and no dilated veins.

Blood-count: Hg. 58 per cent. R. B. C. 4,600,000; W. B. C. 11,600. Differential count: Polys. 78 per cent., lymphocytes 18 per cent., large mononuclears 2 per cent., transitionals 2 per cent. Blood Wassermann on three occasions showed a four plus reaction with the alcoholic antigen and three plus with the cholesterin. Blood urea 0.38 gm. per liter.

Course: On November 22d 5400 c.c. of blood-tinged fluid was removed from his abdomen. A differential count of the cells in this fluid was as follows: Polys. 18 per cent., mononuclears 24 per cent., serosa cells 58 per cent. After removal of the fluid the masses in the abdomen could be made out more distinctly. The upper mass was hard and distinctly nodular. The one in the right side of the abdomen extended almost to the pelvis, was similarly hard and nodular, and was apparently continuous with the upper mass. A similar mass could be made out on the left side extending only part way to the pelvis.

Urobilin in urine: 1644 dilution units.

Stool: Negative for blood. Bile present. No ova or parasites.

Gastric expression: No fasting contents obtained. Ewald test-meal showed no free HCl. Total acidity 14. No lactic acid.

On November 28th 4600 c.c. of fluid removed from the abdomen. This was even more hemorrhagic than before. Again on December 10th 7000 c.c. of hemorrhagic fluid was withdrawn.

Following this last paracentesis the masses could be palpated more easily, were tender, and apparently all connected with the liver.

Several examinations of the urine showed a specific gravity of 1018-1031, generally a very faint trace of albumin, bile on one occasion, a trace of sugar twice, and once a few granular casts.

x-Rays showed no lung metastases, normal cardiac shadow, and nothing definite to indicate a new growth of the stomach or intestines.

His course was essentially afebrile, anorexia was marked, loss of weight was rapid, but there was no vomiting.

On the night of December 12th his condition was apparently unchanged. He suddenly became pulseless, breathing became slow, and he died within twenty minutes.

Autopsy 9183 (Dr. Blake).—Anatomic diagnosis: Cirrhosis of liver; carcinoma of liver, with invasion of portal vein; chronic passive congestion of spleen and pancreas; ascites; rheumatic endocarditis—mitral; rheumatic myocarditis; obsolete pulmonary tuberculosis; fibrous pleural adhesions.

The *liver* is considerably enlarged, weighing 3600 grams. The entire surface is made irregular by rounded nodules and bosses of varying size, some measuring as much as 2 cm. in diam-

eter. On section the normal lobulation is nowhere to be seen. The entire surface appears made up of oval and rounded masses of pale yellow or yellowish-gray tissue. Encircling and separating these nodules are bands of connective tissue. Some of these masses of tissue are more friable than others, and can be readily scraped away; some are distinctly bile stained. The more friable nodules often lie within large veins, and the portal vein is hugely distended with a mass of crumbly tumor extending downward almost to the origin of the vessel (Fig. 1). The gall-bladder is negative.



Fig. 1.—Autopsy 9183. Cirrhosis and carcinoma of liver. Extensive involvement of portal vein.

The inferior vena cava is not invaded. The abdominal cavity contains 2000 c.c. of clear amber fluid. The spleen is enlarged, weighing 760 grams.

Histologic Examination.—The sections show an abundance of connective tissue in the portal regions, with many proliferating bile-ducts. There are large irregular masses of liver cells which appear recently regenerated; they are pale staining, their nuclei are moderately hyperchromatic, the cytoplasm seldom contains pigment. These masses of liver cells bear no constant relationship to the efferent veins; at times there are two or three veins in one mass, and again there is no vein present. In a few areas

in which the liver cells are more deeply pigmented there are distended bile canaliculi between them. Scattered in an irregular fashion throughout the section are liver cells which are larger and more irregular in size than those just described. These cells, while having nuclei containing more chromatin than nuclei of the other cells, do not show a very marked variation from them. Yet in other places there are found large masses of cells frequently arranged in cords like liver cells, at times grouped about one or more efferent veins as are the masses of parenchyma cells,

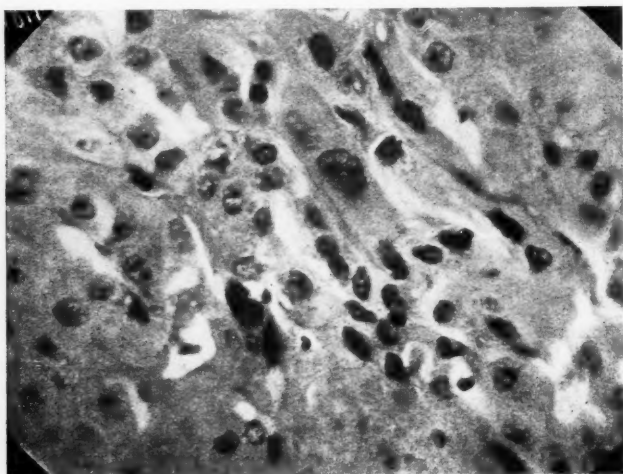


Fig. 2.—Autopsy 9183. Carcinoma of liver. The tumor cells are arranged in cords after the manner of liver cells.

yet these cells show a further variation from the normal. The cytoplasm often takes a more basic stain; in other places it seems paler and less granular. The nuclei of these cells are also less typical. They are usually larger, very hyperchromatic; oftentimes more than one nucleus is found in a cell, or a single nucleus may be three or four times the size of the average liver cell nucleus (Fig. 2). Many of these nuclei contain a very large deeply staining nucleolus. In many places these atypical cells are found growing against and compressing some of the liver cells, and the

difference in their appearance is accentuated where they come into contact. Still the tumor cells bear a distinct resemblance to the liver cell both in general appearance and arrangement. The stroma of the tumor is scant, the vascular supply is fairly abundant in many parts, and the cells are often arranged adjacent to capillaries quite after the fashion of liver cells. Tumor frequently fills branches of the portal vein. In the connective tissue around the portal areas phagocytes containing hemosiderin are in places collected together; they are usually near areas of hemorrhage.

Case II was a Swiss liquor dealer, aged fifty-seven, who was admitted January 2, 1922 and died on the 11th of the following month.

About one month before entering the hospital he noticed that his abdomen was increasing in size gradually and that he was having dragging pains in the upper abdomen. The swelling was progressive and associated with anorexia, morning nausea, loss of strength, dyspnea on exertion, and increasing constipation.

He had been a consistent drinker all his life, but had enjoyed good health. At thirty he had had a neisserian infection, but, so far as he knew, had never had lues. His mother died of cancer of the cervix of the uterus.

The patient was somewhat pale, not jaundiced, with fairly good maintenance of weight and nourishment. The abdomen was moderately distended, with some bulging in the flanks, a fluid wave and shifting dullness, slightly tender in the upper part. After paracentesis the hard, firm liver edge could be palpated, extending slightly more than half-way to the umbilicus. In the right flank the liver edge felt nodular. It was thought that the firm spleen could be felt at the costal margin.

The heart appeared definitely enlarged to the left, with a wide base. Action regular. Aortic second sound loud and sharp. Systolic murmur at apex and over pulmonic area. Blood-pressure 108/74.

The only other findings of importance were a small corneal opacity in the right eye, a pea-sized lymph-gland just above the left clavicle, and absent knee-jerks.

Blood-count: Hg. 90 per cent. R. B. C. 4,400,000; W. B. C. 5600. Differential: Polys. 74 per cent., large mononuclears 17 per cent., lymphocytes 7 per cent., transitionals 2 per cent.

Blood Wassermann: Alcoholic ++; cholesterin ++.

Blood urea: 0.18 gm. per liter.

Blood uric acid: 3.2 mg. per cent.

Blood cholesterol: 0.17 per cent.

Gastric analysis: No fasting contents. Ewald test-meal showed no free HCl, total acidity of 30.

x-Rays showed no evidence of malignant disease of the stomach or intestine.

Course was essentially afebrile. On the day after admission 5250 c.c. of fairly clear dark straw-colored fluid was removed from the abdomen; specific gravity 1014, cells mostly lymphocytes, with a few large irregular shaped mononuclears.

January 11th: Blood Wassermann: Alcoholic \pm , cholesterin \pm .

January 16th: Anorexia and weakness progressive. Rapid reaccumulation of abdominal fluid; 7500 c.c. of light straw-colored fluid removed. Following this the liver edge could be made out 13 cm. below the costal margin in the midclavicular line. It was very hard and two or three very definite nodules could be made out.

Anorexia continued, and periods of nausea, sometimes with vomiting, developed. Loss of 8 pounds since admission.

January 31st: A definite, though slight, jaundice was noted for the first time. Veins on the abdomen more prominent. Liver not tender, and size unchanged.

February 7th: Has had almost continuous nausea and marked weakness. Liver smaller, only 9 cm. below costal margin. Blood-pressure 85/65. Blood urea 0.92 gm. per liter. Non-protein nitrogen 67.7 mg. per cent. Blood-count: W. B. C. 14,000; polys. 79 per cent.; lymphocytes 21 per cent.

The urine showed a specific gravity of 1018-1022, generally a very faint trace of albumin, and on several occasions hyaline and granular casts.

February 11th: Died of what appeared to be cholemia.

Jaundice was never very marked.

Autopsy 9210 (Dr. Blake).—Anatomic diagnosis: Cirrhosis of liver; carcinoma of liver; splenomegaly; ascites; atheroma of aorta; syphilitic aortitis; renal calculi; fibrous orchitis.

The peritoneal cavity contains 5 liters of clear yellowish fluid. The veins in the round and suspensory ligaments of the liver are dilated.

Liver weighs 2610 grams. The surface is coarsely nodular, the nodules measuring usually 0.5 to 1 cm. in diameter. The consistence is increased and there is unusual resistance on section. The cut surface is made up of oval and rounded nodular masses of yellowish-white tissue. In the left lobe the nodules remain discrete, and in between them can be seen occasional remnants of pale brown liver parenchyma. A few dark hemorrhages are present. In the right lobe the nodules are less discrete; they become confluent, forming a more or less solid mass. Connective tissue is increased throughout the liver. There is no invasion of the portal vein (Fig. 3). The gall-bladder, larger bile ducts, and the inferior vena cava are negative.

Histologic Examination.—The connective tissue is greatly increased in the portal areas, and numerous bile-ducts are pres-



Fig. 3.—Autopsy 9210. Cirrhosis and carcinoma of liver.



Fig. 4.—Autopsy 9210. Carcinoma of liver; note contrast between tumor and liver cells.

ent, which frequently give the impression of budding. Large islands of pale liver cells of irregular size are seen; the cytoplasm of these cells often stains intensely with eosin, and the nuclei

seem somewhat shrunken and pyknotic. These nodules are enclosed by connective tissue. Usually there is no definite relation of these masses of cells to the efferent veins. A few areas of hemorrhage are found. Frequently within the margin of these masses of liver cells there are encountered cells which are larger and more irregular in size, whose nuclei are larger, frequently containing a large nucleolus, and the chromatin material in these nuclei is more abundant than in the liver cell (Fig. 4). Some of these

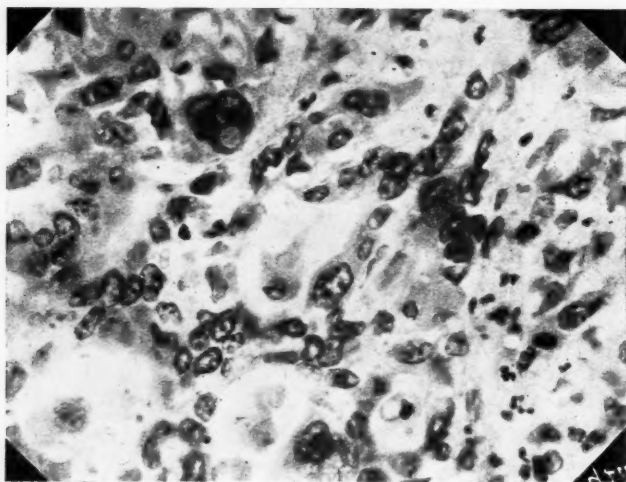


Fig. 5.—Autopsy 9210. Carcinoma of liver. Cells with multiple nuclei. Small spaces enclosed by the tumor cells.

cells are multinucleated. The cytoplasm is relatively less in amount than that of the liver cells and it takes a faint basic stain. In some places it seems possible to trace the connection between tumor cells and cords of liver cells, but whether there is a gradual transition from the latter into the former cannot be definitely stated. In some parts these cells enclose small spaces (Fig. 5). The stroma in many places is quite abundant in between the tumor cells. At times solid columns of multinucleated tumor cells lie in the dense connective tissue in the

portal areas. There is no production of bile in the tumor. No distended bile canaliculi are seen among the liver cells. Into some of the smaller branches of the portal vein the tumor is penetrating and extending along the intimal surface as a single layer of cells. Thrombi in some of these veins are being invaded by the tumor.

The tumor cells resemble in appearance the liver cells; the invasion of the veins is not a prominent feature, and the finding of the masses of tumor at the periphery of the irregular nodules of regenerated liver cells, walled in on the one side by the connective tissue of the portal areas and apparently continuous with the liver cell cords, is of considerable interest. The tendency to enclose small spaces is not striking.

Case III was that of an old man aged seventy-three who lived only eighteen days after entering the hospital on November 1, 1922.

Six weeks before admission he noticed swelling of his legs at night, and two weeks later he found that his abdomen was growing larger. Associated with this there was constant dull epigastric pain, increasing weakness, and dyspnea. His appetite remained good and bowels regular.

He had been a constant user of alcohol all his life, and about six years before he had been told that his liver was enlarged and rough.

As a youth he had gonorrhea and a chancre, untreated except by cautery, followed by secondary manifestations.

For twenty years he had had a mild diabetes, and for about eight years he had been troubled by exertional dyspnea and palpitation.

Physical examination showed a well-preserved and nourished old man with florid complexion and numerous angiomas—not jaundiced.

The abdomen was large and protuberant, with bulging in the flanks and shifting dullness. A very much enlarged liver was felt extending about half-way to the umbilicus. It was hard and firm, only very slightly tender, and not nodular. It was thought that the spleen could be felt just at the costal margin.

In addition, he showed general arteriosclerosis, pupils which did not react to light, bilateral hemianopsia, bad teeth, an enlarged heart without murmurs, blood-pressure 140/65, left fibrous orchitis, and absent knee-jerks. Blood-count: R. B. C. 4,900,000; W. B. C. 9600; polys. 67 per cent., lymphocytes 26 per cent., eosinophils 6 per cent., basophils 1 per cent. Urine: 1026, acid, no albumin, no sugar, very few hyaline casts.

Course was afebrile.

Blood Wassermann: Alcoholic 0, cholesterin \pm .

Blood-sugar: 1.19 gm. per liter.

Blood urea: 0.11 gm. per liter.

Blood uric acid: 2.5 mg. per cent.

November 3d: Paracentesis; 3500 c.c. of slightly turbid yellow fluid; specific gravity 1018, cells 120 per cubic centimeter, albumin 12 grams per liter, culture no growth.

November 7th: Bile present in urine, and three days later definite icterus noted.

November 9th: Blood-sugar: 1.42 gm. per liter.

Blood CO₂: 50 vol. per cent.

November 12th: Bile present in stool.

November 14th: Paracentesis; 5800 c.c. opalescent fluid; specific gravity 1.008, albumin 9 grams per liter, cells 145.

Following admission specimen, bile was constantly present in the urine, and there were traces of sugar which yielded readily to mild carbohydrate restriction.

Reaccumulation of fluid after the paracentesis of November 14th was rapid, but did not necessitate another tapping.

He became irrational, then comatose, and died on November 19th.

Autopsy 9317 (Dr. Frantz).—Anatomic diagnosis: Cirrhosis of liver; hemosiderosis of liver; carcinoma of liver, with invasion of portal and hepatic veins; extension to inferior vena cava; metastases in lungs; thrombosis of portal vein; ascites; arteriosclerosis, with calcification of coronary arteries; fibrosis of myocardium; fibrous orchitis—left; acute prostatitis.

The peritoneal cavity contains 2400 c.c. of clear straw-colored fluid. The veins in the various ligaments of the liver are dilated.

Liver weighs 1670 grams. The surface of the right lobe is rather finely nodular, the nodules being fairly uniform in size and about 3 mm. in diameter. The inferior half of the left lobe presents the same appearance. In the upper half of the left lobe the capsule is lifted up by a large flat mass of yellow color, and nearby are several smaller, similar masses. The large mass is 10 x 6 cm. in diameter, and the capsule over it is considerably thickened. About the periphery of the nodules are many dilated vessels in the capsule. On the inferior surface opposite these masses are other similar nodules, and frequently the very small vessels lying either in or just beneath the capsule are distended by tumor, and the various branches can be easily followed, as though they had been injected with tumor.

On section the cut surface is slightly rust colored and does not appear jaundiced. In the left lobe is found the tumor made

up of rounded masses of friable yellow tissue, often surrounded by a definite thin gray wall. In places the tumor quite clearly is distending the veins; in other areas the outline is not so well defined (Fig. 6). In some of the larger masses of tumor are fragments of thrombus. The liver tissue adjacent to these masses is compressed. The cut surface of the left lobe is somewhat paler than that of the right. In the remaining portion of the left lobe, away from the tumor and in the right lobe, the normal lobulation is not to be seen. Instead are small rounded or oval nodular masses of liver parenchyma, yellowish brown in color, with delicate bands of connective tissue about them. The branches of the portal vein in the right lobe are filled with dark red, friable thrombi, with occasionally a small plug of

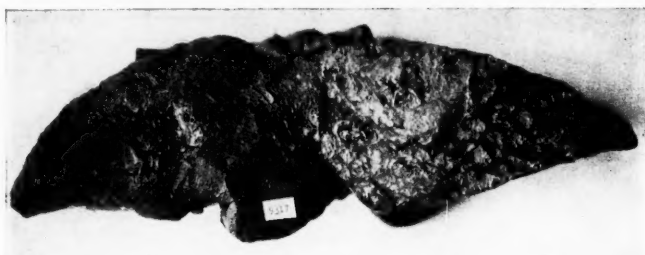


Fig. 6.—Autopsy 9317. Cirrhosis and carcinoma of liver. Marked invasion of portal veins.

yellow tumor tissue in the midst of the thrombus. The left branch of the portal vein is greatly distended with tumor. The portal vein and its right branch are filled with a thrombus. The upper part of the inferior cava is distended with a solid tumor mass adherent to its wall and just reaching to the right auricle. The surface of the end of the tumor plug is for the most part smooth and is apparently covered over with endothelium, except in the central portion.

Lungs.—In both lower lobes are found a few firm grayish-white nodules, varying in size from 1 mm. to 1 cm. These are for the most part close to the pleura. They are sharply demarcated from the surrounding lung tissue.

Histologic Examination.—There is a very definite increase in connective tissue in the portal regions, and in many places the bile-ducts are quite obviously proliferating. There are irregular masses of liver cells without the normal arrangement in lobules. These cells are frequently pale, and have within them a coarse brown pigment which gives a positive reaction for iron. Many phagocytes containing hemosiderin are to be found in the connective tissue in the portal region. The liver cells show a slight variation in staining reaction. The nuclei are fairly uni-



Fig. 7.—Autopsy 9317. Carcinoma of liver.

form in size and contain a small amount of chromatin. The cytoplasm in some places stains intensely with eosin. In other places it takes a faint stain with hematoxylin. The epithelium of the bile-ducts also contains some hemosiderin.

The tumor is composed of cells having slightly larger nuclei than those of the liver cells, rounded or oval in outline, and containing a little more chromatin than the liver-cell nuclei (Fig. 7). The amount of cytoplasm is relatively less as compared with the size of the nucleus than that of the liver cell. The cyto-

plasm of the tumor cells takes a faint basic stain in many places; in other places it takes no stain at all, and appears quite clear and finely granular. The tumor cells grow in large masses with little stroma. The central parts of these masses have frequently undergone necrosis. There is very active invasion of the portal vein and here the tumor grows in a somewhat different fashion. There are apparently long streamers of tumor cells which anastomose with other streamers, and the surface of these is covered with a single layer of endothelial cells, and in the space is well-

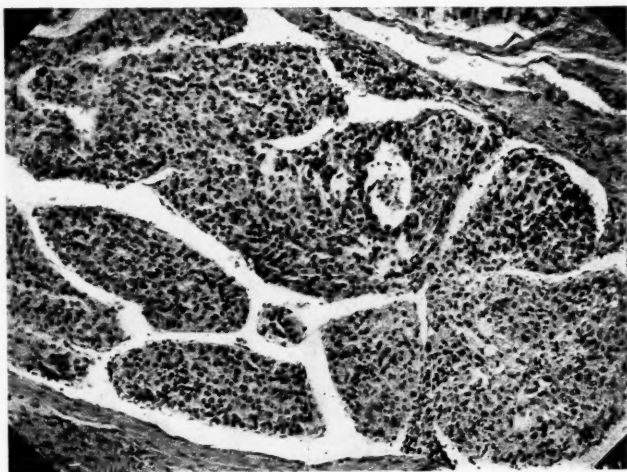


Fig. 8.—Autopsy 9317. Carcinoma of liver. Masses of tumor in portal vein covered with a single layer of endothelium.

preserved blood (Fig. 8). There are encountered in different portions of the tumor multinucleated cells with very clear cytoplasm (Fig. 9). Mitoses are rare, though occasionally very hyperchromatic nuclei are present. The tumor cells do not grow in cords after the fashion of liver cells, and yet in many places, where the cytoplasm takes a faint stain with hematoxylin, they resemble very closely the liver cells in appearance. In a few areas the tumor cells are apparently invading adjacent masses of liver cells, but there is not the appearance of a gradual

transformation from the liver cells to the tumor cells. Many polymorphonuclear leukocytes are present in the portal regions.

In sections from the right lobe there are irregular nodules of pale staining liver cells lying beside equally irregular masses of smaller liver cells, taking a rather intense basic stain and containing a large amount of hemosiderin. Connective tissue is greatly increased in the portal areas, and these irregular masses of liver cells are surrounded by bands of fibrous tissue of varying width. There is marked infiltration of the connective-tissue

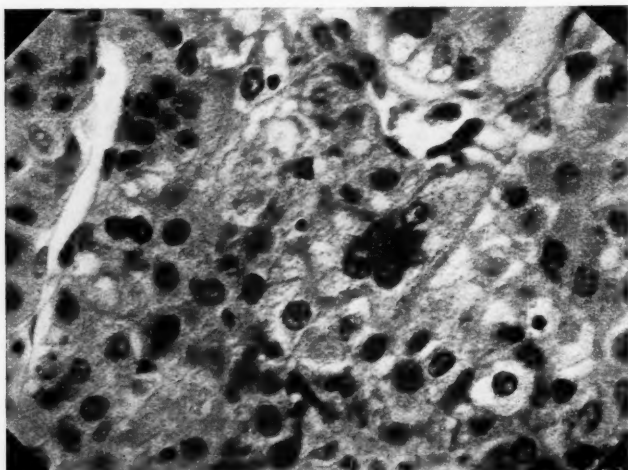


Fig. 9.—Autopsy 9317. Carcinoma of liver. Multinucleated and clear cells.

septa with small wandering cells. A few phagocytes containing hemosiderin are to be seen in the connective tissue. There is no distention of bile canaliculi made out anywhere in the sections.

Lung.—The nodules in the lung are composed of cells identical to those of the tumor in the liver; these cells in places lie free, distending alveolar spaces; in other areas they are definitely within the blood-vessels. The stroma is not abundant. The tumor is only moderately vascular.

Case IV was a man of fifty-four, who entered the hospital February 26, 1923, and died March 9th.

Eight weeks before admission he was in bed for two weeks with slight fever and cough. Diagnosis: Pleurisy.

Five weeks ago, after returning to work, he noticed considerable swelling of his abdomen and general abdominal discomfort, most marked in the right upper quadrant, aggravated by any food except fermillac. No nausea or vomiting. Bowels kept open with cathartics; no bloody, tarry, or clay-colored stools.

At about the same time he began to have swelling of his legs, weakness, and exertional dyspnea.

For three days before admission he had moderate jaundice.

At the age of three he had smallpox. At the age of twenty-one he drank heavily for three years. Since then very little.

Physical examination showed a poorly developed, slightly jaundiced man, with intermittent hiccup. There were telangiectases over nose and thorax, and a few dilated veins over the lower thorax.

The abdomen was distended and showed shifting dullness and a fluid wave. The smooth sharp liver edge was felt about 2 inches below the costal margin, in the midclavicular line; not tender. Spleen was not felt.

In addition to the above there was edema of the back and lower extremities, a small amount of fluid in each chest, slightly irregular, sluggish pupils, sluggish knee-jerks, and a soft apical systolic murmur in a normal sized heart.

Blood-count: Hg. 105 per cent.; R. B. C. 5,008,000; W. B. C. 15,200; polys. 76 per cent., lymphocytes 23 per cent., large mononuclears 1 per cent.

Urine: 1023, acid, no albumin, no sugar, a few hyaline and mixed casts and W. B. C.

Course was afebrile, with terminal rise to 101° F.

Wassermann: Alcoholic negative, cholesterin negative.

Tetrachlorophthalein liver function test: 0.2925 gm. of dye injected.

Normal.

Blood-serum after fifteen minutes = 15 per cent. dye 6 per cent.

Blood-serum after sixty minutes = 23 per cent. dye 3 "

Serum contained considerable bile-pigment.

March 2d: Has grown progressively worse. Continuous hiccup for past twenty-four hours. Jaundice has deepened and he has become increasingly more drowsy. Ascites has become decidedly less in amount.

March 9th: Jaundice has deepened, complete coma for past week. Died March 9th.

Autopsy 9364 (Dr. VonGlahn).—Anatomic diagnosis: Cirrhosis of liver; jaundice; carcinoma of liver, with invasion of portal vein and inferior vena cava; thrombosis of inferior vena cava; edema of legs; submucous and subepicardial hemorrhages; acute bronchitis; lobular pneumonia; edema of lungs; hyalinization of islands of Langerhans.

Liver weighs 1300 grams. The veins in the various hepatic ligaments and over the right half of the peritoneal surface of the

diaphragm are dilated. The surface of the left lobe of the liver is slightly irregular; over the right lobe the capsule is lifted up by rounded, moderately flat nodules which vary in size up to 1 cm. in diameter (Fig. 10). These nodules appear grayish yellow, while those seen in the left lobe are somewhat greenish in color. The capillaries in the capsule are prominent.

The liver cuts with greatly increased resistance. In the right lobe is an irregular mass of friable grayish-yellow tissue which is apparently made up of nodules which have become more or less confluent. Some of the masses of tumor are definitely held

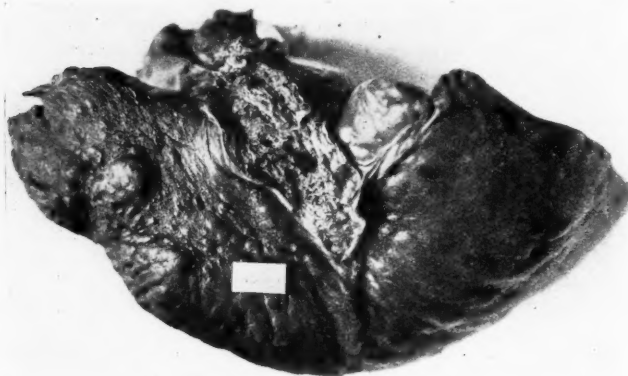


Fig. 10.—Autopsy 9364. Cirrhosis and carcinoma of liver. Masses of tumor in right lobe. Inferior vena cava filled with tumor.

within a capsule, are oval in outline, and give the impression of tumor filling and distending blood-vessels. This is especially true of one large mass, and this mass, when traced downward, is found to be filling a branch of the portal vein (Fig. 11). There is no lobulation made out in the tumor. The parenchyma in the right lobe in places is pressed upon by the tumor. Elsewhere the lobulation is irregular, and there is some congestion and bile staining. Also there are found small oval grayish nodules which are not so yellow as the tumor, which sometimes are slightly bile stained, and which are often partially surrounded by com-

pressed, deeply bile-stained, crescentic masses of liver tissue. These give the impression of nodules of regenerated liver. In the left lobe the lobulation is totally irregular, bands of connective tissue are everywhere present, surrounding nodules of parenchyma of varying size. There is much stasis of blood and deep jaundice, which gives the cut surface a striking appearance of alternating hemorrhage and bile staining. The cut surface of the left lobe is also dotted with yellow flecks as though some of the cells contained fat. Everywhere the veins are distended with dark red thrombi. The right branch of the portal vein, in



Fig. 11.—Autopsy 9364. Cirrhosis and carcinoma of liver. Tumor filling and distending large branch of portal vein.

addition to the plug of tumor projecting into it, is almost completely occluded with a laminated grayish-red thrombus. The main branch of the portal vein to the left lobe is free, but many of the smaller branches contain thrombi. The hepatic veins are infiltrated with tumor, and the terminal portion of the inferior vena cava is occluded and distended by a grayish-yellow, bile-stained, friable plug of tumor which projects into the right auricular cavity as a bluntly rounded mass with a fairly smooth surface (Fig. 10). The intima of the cava seems to be reflected upon and over the end of the tumor mass. The first portion of the cava is filled with a soft, friable, laminated thrombus.

The gall-bladder and ducts are negative.

Other findings were a moderately enlarged spleen, dilatation of the veins in the lower part of the esophagus, and bile staining of the various organs.

Histologic Examination.—Sections from the left lobe reveal oval and rounded masses of liver cells, frequently without an efferent vein; these cells are often of unequal size and stain faintly. Others of these masses of liver cells have within them several efferent veins, and about these vessels hemorrhage is

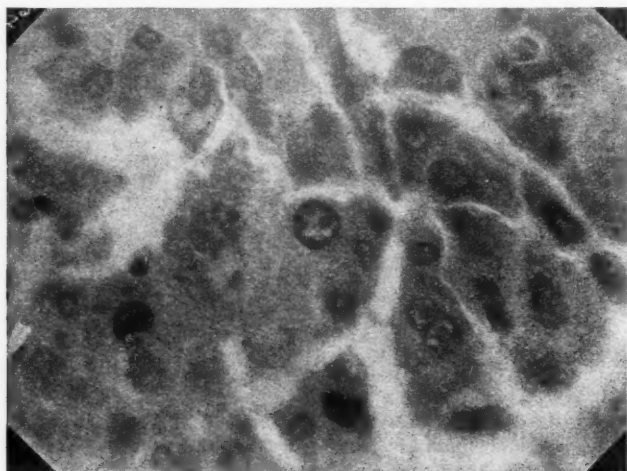


Fig. 12.—Autopsy 9364. Carcinoma of liver. The tumor cells closely resemble liver cells.

present. Distention of bile canaliculi is marked; this is especially seen where the liver cells are smaller, more deeply pigmented, and seemingly not so recently regenerated. Connective tissue is increased in the portal regions, and proliferating bile-ducts can be followed until they join the islands of liver cells. The portal areas are infiltrated with small wandering cells, occasional eosinophils, and a few polymorphonuclear leukocytes.

In sections from the right lobe the changes described above are to be seen. Also there is a tumor made up of cells larger than

the liver cells; often these are polyhedral in outline, though at the periphery of the mass they are at times somewhat columnar. The nuclei are rounded or oval, with distinct outline; they are generally larger and contain more chromatin than the liver-cell nuclei. Many of the nuclei are very large, being several times larger than the nuclei of the liver cells. These large nuclei have usually a prominent deeply staining nucleolus. The cytoplasm is variable in amount; it is usually more abundant and stains more intensely with the basic dye than does that of the liver cells (Fig. 12). Cells with multiple nuclei are numerous. Mitoses are not found. The tumor is growing in large masses; its cells are not arranged in cords, and it compresses the surrounding liver cells where it comes into contact with them. Yet the cells resemble closely the liver cells. There is very little stroma made out in the tumor. Many veins are filled with the tumor; some of these can be readily identified as branches of the portal vein, others are efferent vessels.

The mass in the inferior cava is quite identical to the tumor in the liver and the resemblance to liver cells is rather striking.

Necrosis has occurred in the nodules of tumor in the liver and cava.

No metastases could be found.

PATHOLOGIC DISCUSSION

These 4 cases are examples of carcinoma of the liver having their origin from the liver cells. The occurrence of such tumors is not frequent.

In the last 1800 autopsies at this hospital there have been 6 cases; of these, the 4 presented here occurred within a period of two years. The incidence in our small series is 0.33 per cent. These figures agree with those of Goldzieher and v. Bokay, but are higher than those of Orth (0.028 per cent.).

The majority of liver-cell carcinomata are found in men and are most numerous after the age of forty. Examples have been reported in children, and are believed to have arisen from adenomata. Griffith collected 57 cases in children under the age of sixteen.

The size of the liver is variable. In 3 of our cases it was considerably enlarged; in the other case it weighed somewhat less than normal. This enlargement contrasts strikingly with the usual size of the liver in advanced cirrhosis. Jaundice is variable; it may be intense, moderate, or entirely wanting. The gross appearance is usually sufficiently striking to permit easy separation from the changes following cirrhosis. The tumor is generally more friable and grows often in larger masses than the regenerated nodules of liver tissue. Invasion of vessels by the tumor is common. Deep jaundice of the liver with light bile staining of the tumor will further accentuate the difference. Occasionally where the tumor process is more diffuse, as in Case II, the differentiation from nodules of regenerated liver cells may be more difficult. Yet there is a tendency for tumor masses to become confluent, while the nodular masses of regenerated liver cells remain discrete.

In all of our cases there was cirrhosis of the liver, and most of the carcinomata of the liver in adults are in cirrhotic livers. The tumor appears to be secondary to the cirrhosis, as maintained by Sabourin, and the cirrhosis may be of any type. Cases are reported of carcinomata following cirrhosis of syphilitic and parasitic origin, as well as after the simpler types. In a few of the cases there has been hemochromatosis. In one of our cases large amounts of hemosiderin were present in the liver.

In 3 of the 4 cases presented here (Cases I, III, and IV) the cirrhosis undoubtedly preceded the tumor. The cirrhotic process is equally advanced in those parts of the liver not involved by the tumor, and it does not seem reasonable to regard the connective tissue increase at distances from the tumor as secondary to the tumor. In the other case (Case II), where the tumor is more diffuse, the question might be raised that the cirrhosis followed the tumor. This is unlikely, for the regeneration and cirrhosis are out of all proportion to the amount of tumor present. The carcinomata arising from the bile-ducts are less often associated with cirrhosis.

The main point of contention in these carcinomata of the liver is whether they are unicentric in origin, or spring from

more than one focus, that is, of multicentric origin. Ribbert advanced the theory that they are of unicentric origin, and that the dissemination in various parts of the organ resulted from the invasion of the portal veins. This view has been held by many observers since, and it has been claimed by some that when the mass of tumor is removed from the portal veins most of the tumor nodules are removed.

Three of these cases (Cases I, III, and IV) suggest a unicentric origin. The tumor mass in each instance is more or less sharply localized to one lobe. There is massive involvement of the portal vein by the tumor, and many of the nodules can be seen definitely to lie within branches of the vein.

In the other (Case II) a unicentric origin is more difficult to uphold. There is no macroscopic invasion of the portal vein, and the microscopic involvement of the vessels is very slight. The tumor is very wide-spread throughout the liver, and histologically it is generally situated at the margin of the nodular masses of parenchyma, with a wall of connective tissue on one side, while it merges with liver cells on the other. The transition between the liver cells and tumor is often very gradual. The theory of multicentric origin was advanced by v. Heukelon, and in this case it would seem the more reasonable view. If the regeneration of cells exceeds the limits of physiologic necessity and results in a tumor, there is no reason to suppose that such an impetus might not operate in more than one portion of the organ.

In addition to the invasion of the portal veins, these tumors readily penetrate into the hepatic veins, and may extend into the inferior cava or even into the right auricle of the heart. Two of our cases show this feature, the end of the tumor plug being more or less completely covered with endothelium continuous with that of the vessel.

The tumor cells may be arranged in fairly solid masses or in columns, recalling the cords of liver cells. Rarely is there the formation of lumina. In such spaces may be found bile or cell debris.

The tumor cells, as a rule, are easily distinguishable from the

liver cells by their staining reaction; generally the cytoplasm of the tumor cell is more strongly basophilic than that of the liver cell. At times the cytoplasm of the tumor cells fails to take any stain and appears quite clear. The nuclei are usually larger and more hyperchromatic than liver-cell nuclei, though the general shape is the same. Mutinucleated cells are not infrequent and mitoses may be found. The stroma is scant; the vascular supply is variable and necrosis may be wide-spread. Bile is sometimes produced by the tumor.

Notwithstanding the striking tendency to invade the hepatic veins, secondary nodules outside the liver are not of frequent occurrence. Only one of these cases showed metastases, and these were in the lung. In some cases metastases have been present in lymph-glands.

CLINICAL DISCUSSION

You have had pointed out to you the fundamental pathologic changes which occurred in these beautiful examples of primary carcinoma of the liver. This is the most essential part of today's conference, as it is the basis upon which you must build a clinical picture of the disease, a picture, which up to the present time, is by no means clear cut.

We are dealing with an uncommon disease. As we have pointed out before, there is no harm in suspecting and in trying to run to earth the rarer conditions in medicine. In fact, medicine loses much of its interest and charm if we proceed merely along the path of a mechanical doctrine of chances. There is, however, the necessity of warning that one must be constantly on guard and scrupulously careful of every point in arriving at the conclusion that a given condition is better explained by a rarer rather than a more common diagnosis.

The examples of disease which you have seen today are cases in point. All of these cases showed cirrhosis, and it must have been apparent to you all that this was the feature which overshadowed the clinical picture. The temptation of the doctrine of chance would tell us to be content with that diagnosis and to beware of the pitfalls of seeking a rarer explanation. However,

the great majority of the cases of primary carcinoma of the liver show the clinical and pathologic picture of cirrhosis, and if we are to make the diagnosis in even a minority of these, we must take chances along the path of the more unusual diagnosis.

So that the first lesson which we should learn today is that, given a case presenting the symptoms and signs of cirrhosis of the liver, we have given to us also the possibility, at least, of a primary carcinoma in that liver. In other words, the first step in the diagnosis is to keep in the back of your mind the remembrance that there is such a disease, even though it be rare, and that when it does occur, cirrhosis of the liver is the soil in which it usually develops.

Granted this possibility, we should consider next whether such a case presents any features unusual to a straight-forward cirrhosis. And we are struck at once by the fact that all of these livers were enlarged very considerably at a time when in simple cirrhosis with the onset of ascites, one would expect, in most cases, a considerable decrease in the size of the organ. Given, then, the picture of an ordinary cirrhosis with ascites where the liver is quite large or where it increases in size under observation, we have additional evidence to direct our attention to something more than a Laennec cirrhosis, remembering constantly that these are but straws which point the way, as there are no pathognomonic signs of primary carcinoma of the liver.

If, in addition, there be found irregular, single or multiple nodules of the liver, different from the remaining palpable portion, one begins to feel a little added confidence in thinking of the rarer diagnosis. Such was the condition in 2 of these cases, and was of sufficient importance to lead to the suspicion, at least, of the true condition.

Here, however, we run into a block signal which warns us that we are face to face with the problem of liver metastases from some other primary tumor, a very much commoner condition as you know. This means a careful review of all the organs, using the various diagnostic means at our disposal to discover or rule out any other tumor.

You must have been struck by the comparatively brief

course of the illness in each of these cases, a point which has been emphasized by all writers on the subject. The longest duration in our cases was eleven weeks, and the shortest, nine weeks.

I think it would be our general impression that the course of a portal cirrhosis, the condition which causes the most difficulty in diagnosis, is considerably longer than this. However, actual investigation of our autopsied cases shows that the duration of life after the onset of ascites, which corresponds with the date of onset of the cases which you have seen today, was under twelve weeks in the great majority. Consequently we do not feel that we can place much reliance upon the rapidly fatal course.

If you have reached a point in any given case where, along the above lines, you have some ground for suspecting a primary carcinoma of the liver, the discovery of a metastasis in some other part of the body, in the absence of any other discoverable primary tumor, would be of real value. Unfortunately, from the diagnostic standpoint, these tumors are not given to forming distant metastases in spite of their great tendency to invade the adjacent large veins, including the inferior vena cava. In only one of our cases were there metastases. These, as you will remember, were in the lung, the site of election for these metastases when they do occur, but were too small for x-ray detection. However, as they do occur in a few cases, every effort should be made to detect them where the disease is suspected.

Jaundice occurs in some 61 per cent. of the cases. It was present late in all of our patients, but of no considerable degree except in one. It is more marked in secondary carcinoma of the liver.

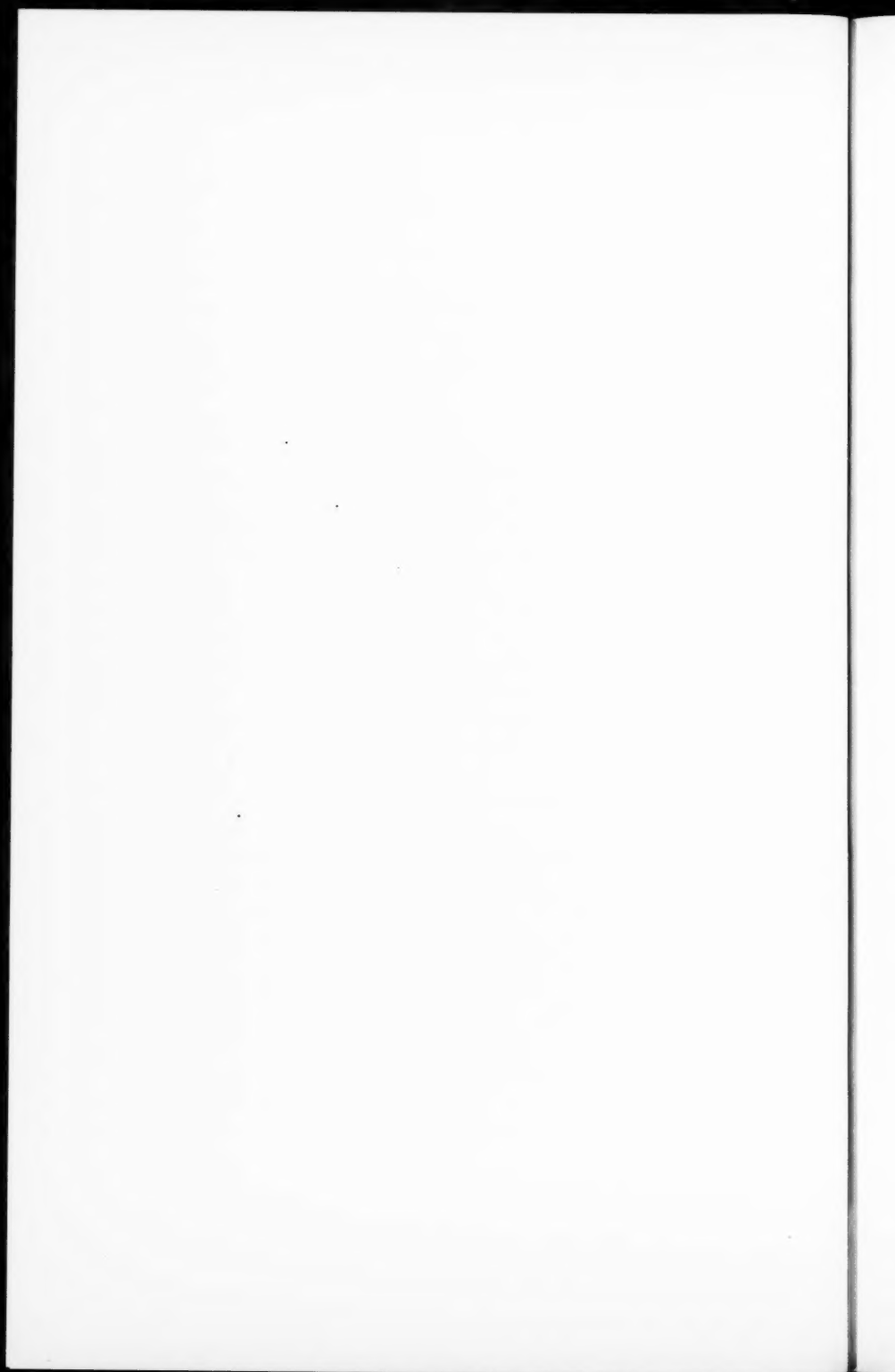
All of the cases here had ascites, hemorrhagic in only one. In collected series ascites occurs in about 58 per cent.

The occurrence of anorexia, gastro-intestinal symptoms, cachexia, splenic tumor, hematemesis, hemorrhoids, edema of the lower extremities, and evidences of anastomotic circulation are of no real value in differential diagnosis, as they are all apt to be part of the ordinary cirrhosis.

The following references which we have put upon the black-board cover the important contributions on the subject.

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CLINIC OF DR. GEORGE DRAPER

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ENDOCRINOLOGY AND PEDIATRICS

YOU have asked me to present to you a consideration of the endocrinology of childhood, and particularly to point out what is actually known about the expressions of pathology of the glands of internal secretion in the early years of life, and what is still only surmised.

Obviously, the problem is an exceedingly difficult one, and I can bring to its solution no new evidence. If it were possible to visualize completely, from without, the working of the complicated glandular mechanism, we would doubtless be in a position to analyze personality to a very great extent. Not having been able to do this, however, many attempts have been made to study personality, and then to explain it by assuming its cause to be the result of certain glandular functional relationships.

We are forced, of necessity, to approach so vast a subject as the human individual piecemeal, although in this problem we are concerned with the whole glandular equipment. This is a mechanism, as you well know, composed of at least seven glands: the pineal, the pituitary, the thymus, the thyroid, the adrenals, and the sex glands; the pancreas in part, perhaps the liver, and it may well be other tissues of the body which have not yet been recognized as producing hormones. These several glands, or parts of the glandular machine, have the closest imaginable relationship, so that it is impossible to discuss disturbances of one gland without being at once involved in a consideration of the changed reactions set up in the other members of the group.

There was a time not so long ago when so-called polyglandular syndromes were described as special clinical entities in them-

selves. Now we are coming more and more to realize that the physiologic disturbances caused by one gland are promptly extended to expressions of polyglandular disbalance. In other words, it is probably not far from the truth to say that uniglandular pathology invariably means polyglandular dystrophy. Obviously, in such a demonstration as this it will be impossible to discuss each gland in its total physiologic and pathologic states, and all the secondary polyglandular disturbances which arise from these. Indeed, one might almost say that the whole of medicine would be compassed in such a discussion.

There are, however, certain general conceptions of the problem which may tend to clarify or at least to offer a way of thinking about the subject with a certain degree of precision not too much blurred by romance. There seem to be two fundamentally important relationships of the glands to the phenomena of life; first of all, there is that which is concerned with the phenomena of growth and development of the individual, and, second, that which is related to the maintenance of the physiologic balance for the remainder of life after the termination of the growth process.

While we are not yet in a position to say definitely that the glands control the activities in either of these groups, we must admit that they hold an exceedingly important relationship to them. For the pediatrician endocrinology is almost entirely limited to the first set of phenomena, namely, those of growth and development.

Life is the expression of continuous cellular activity, but, in addition to those basic processes of the metabolic change which represent living, there are certain other activities which are special to the years, and which seem to mark off the span of life into fairly well-defined epochs. Thus, during the childhood and adolescent periods, different basic cellular activities of the living process go on just as they do throughout the remainder of life, but in addition to these there is also the special activity concerned with growth and development. Growth and development, consequently, are the outstanding, most obvious features of the pediatric period. As a result any spectacular

augmentation in speed or extent of growth and development claims primary attention. Similarly, restraints in growth and inadequacies of development deflect the attention of parents and doctors from what may be called the average to these more unusual forms. Thus, endocrinology for the pediatrician becomes very largely concerned with matters of growth and development. In the adult phase of life, by a similar process of reasoning, endocrinology for the internist becomes largely a part of the study of constitution.

To sum up the expressions of the last paragraph, it may be said, then, that when the growth and development determining functions of the glands cease, their physiologic balance-maintaining function continues in accordance with hereditary influences, on the one hand, and the later effects of environment on the other. There is a vast literature already available to offer explanations for the phenomena which are called endocrine in origin. Some few of these present the evidence of pathologic anatomy in one or more of the glandular structures with correlated descriptions of the clinical aspects of the case; while many more contributors to the literature offer clinical discussions with pathologic surmises. To anyone who has observed the great variety of growth disturbances associated with demonstrable glandular pathology and the remarkable similarity in appearance of many individuals in whom no glandular pathology can be proved, it would be very satisfactory to demonstrate conclusively that the cases without glandular pathology depended upon some functional disturbance of the suspected gland. The only justification for assuming functional disturbance of a gland which does not depend upon anatomic pathology of that gland is the similarity or analogy of the clinical symptoms. In other words, we are faced with the difficult question: Are the pathologic and physiologic precocities (accelerations) and retardations dependent upon the same mechanism, namely, a glandular one—in the former case an anatomic lesion, be it bullet wound or tumor; in the latter, the inherent hereditary quality of gland tissue?

We would all like to believe that our clinical pictures are

dependent on the same mechanism, and the presumptive evidence is undoubtedly very strong that they are. Proof, however, is still lacking. It is a most interesting thing to review the literature of this subject and to see how frequently the same cases have been noted and renoted in illustration of the various supposed forms of glandular pathology.

Cushing's¹ book on Disorders of the Pituitary Body, written in 1912, presents, in addition to his own cases, several taken from the literature. Many of these, both from the literature and from Cushing's series, have been quoted by other authors since. The important and somewhat depressing note in all this repetition is that while these cases still remain incompletely explained, they are being used constantly as patterns of definite glandular pathology. It appears, unfortunately, that today there is but little better understanding of the phenomena of growth and development than there was twelve years ago when this book was written. This lack of real knowledge makes classification very difficult. There is also a confusion and often a misunderstanding of terms. Take, for example, the so-called "Fröhlich type." I think that for most of us who use this term frequently the conception which Fröhlich originally had rarely enters into our thought processes. The title of Fröhlich's papers was A Case of Tumor of the Pituitary Without Acromegaly, and yet we now habitually think of the so-called "Fröhlich type" as the classical little fat boy or fat girl with an outstanding insufficiency of the gonads. In passing, while the title of Fröhlich's paper is still fresh in our minds, it is of interest to call attention to our equally fixed association of tumors of the pituitary with acromegaly.

It will be impossible within the scope of this paper to discuss all the other forms of dwarfism, just as it would be impossible to discuss all the various forms of gigantism and adiposity. Consequently, a consideration of thymus disturbances, adrenal disease, and thyroid deficiencies will be omitted. The last group, with cretinism as its classic expression, is, of all the disturbances of glandular mechanism, the one which is perhaps most firmly established both on a pathologic and clinical basis. That this

condition is definitely related to the thyroid gland there can no longer be any doubt. Consequently we feel perhaps a greater sense of confidence in approaching these cases than we do those of any other type of glandular disturbance. But there is one group of case which has seemed to me to be, perhaps, the most confused of all. This is the broad group, including various forms of infantilism cases and of adiposity with gonadal insufficiency.

The latter group has been discussed by R. Neurath,² under the excellent and non-committal title, *Fat Children*. Cushing differentiates two types, the first of these, the so-called Fröhlich type, in which there is infantilism both structural and visceral, with adiposity of the juvenile type in the presence of a pituitary tumor. The other type is represented by his Cases XXXIII and XXXIV, in which there is structural gigantism which he attributes to anterior lobe hyperplasia, with genital hypoplasia characterized by some disturbance of fat distribution, epileptoid seizures, but with an absence of pituitary tumor. The picture (Fig. 13), borrowed from Cushing's book, represents his Case XXXIII, showing the type which he has described as differing from the classical Fröhlich type in being very much larger so far as skeletal development is concerned. The condition in this case is the result of physical trauma occasioned by the child's falling downstairs as a baby.

Neurath believes that it is justifiable to assume, as a result of the combination of clinical and pathologic observations that have been gathered, that the excess fat in these children results from defects of the pituitary gland and sex gland. It is interesting to observe, however, that he reports in connection with this statement a case without pituitary disturbance, but with a tumor of the cerebellum. Nevertheless, he still ascribes the condition to interference with the function of the pituitary gland due to the hydrocephalic pressure. There was also epilepsy in this case. Even so good an observer as Neurath felt it necessary to advance this explanation of an indirect mechanism affecting the pituitary function.

Frankl-Hochwart,³ in discussing tumors of the pituitary gland, believes that in males practically all show underdevelop-

ment of the genitalia with a tendency to increased breast size; and that in females a similar genital aplasia or hypoplasia is usual. However, he did see 3 cases in which there was an overdevelopment of the sex glands. In his review of the literature of pituitary tumors he was surprised to find that general adiposity was not always present, for there were 16 cases reported in

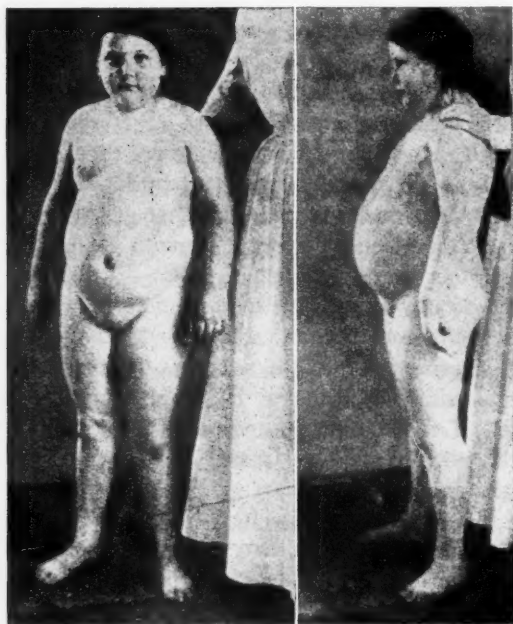


Fig. 13.—Case of adiposity, structural overgrowth, and epilepsy due to trauma, originally shown by Cushing in 1912 as Case XXXIII.

which a loss of weight was described. He quotes Marburg as stating that the age at which the tumor starts determines the extent of development. This author believes that the younger the case is at the time the tumor begins, the greater the chance for the development of abnormal fat. Hochwart makes the statement that fat and genital hypoplasia almost always are found in common. He makes this statement notwithstanding

the fact that he has 4 cases in which this combination is not present. These cases all had genital deficiencies, but no increase in fat.

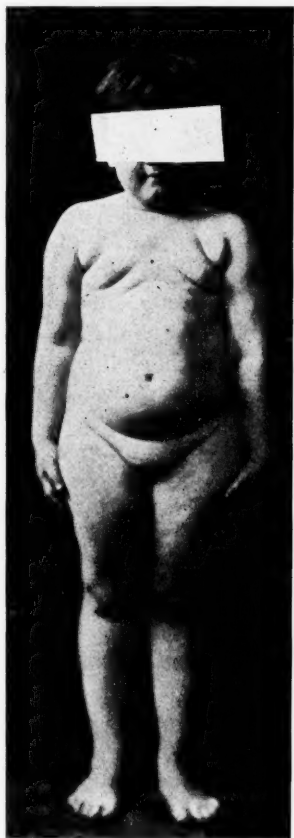


Fig. 14.—Fat child of unexplained glandular pathology.

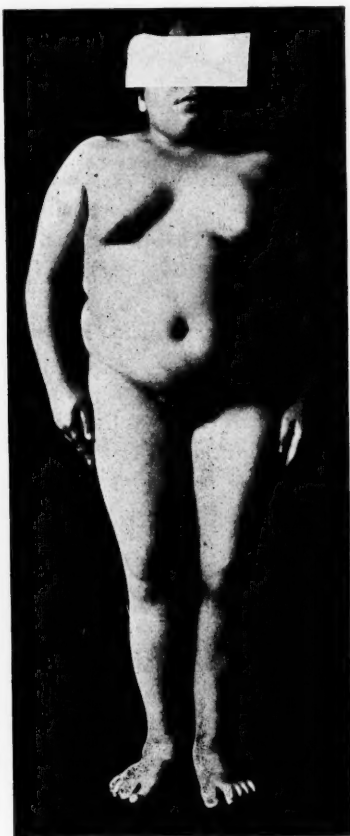


Fig. 15.—Fat child of thirteen and a half years. Unexplained glandular pathology. Unusual mental development.

Figures 14 and 15 are cases which have been under our observation at the Presbyterian Hospital. Figure 14 is of a child

five years of age. We have been unable to make a diagnosis, and so we have thrown her into the convenient category of the Fröhlich type. At the age of five years she weighed 60.5 pounds and was 43 inches high. Obviously, she belongs rather in the group described by Cushing and shown in Fig. 13. Figure 15 is an individual thirteen and a half years old. She had a most unusually mature and alert mentality, and gave one the impression of being at least seventeen or eighteen years old in her grasp of any situation which might be under discussion. Another interesting feature of this case was the fact that her basal metabolism was +22. Yet, notwithstanding this finding, and her great speed of mental reaction and general alertness, she maintained her excessive weight. Obviously these cases have been classified "Fröhlich" simply because of their external contours which display the characteristics described by Fröhlich and others who have associated the condition with pituitary disturbance. Radiographs of the heads of these patients failed to show any disturbance of the pituitary fossa or other signs of intracranial disease.

Since we have been studying at the Presbyterian Hospital the morphology of human beings by the more careful technic of the anthropologist we have on several occasions been surprised to find how great a discrepancy may exist between skeletal development and fat distribution and development. Figures 16 and 17 show a case which was sent to the clinic as one of precocious sex development. The diagnosis was based upon the fact that in a child aged eleven and a half years who had already begun to menstruate there appeared all the physical characters that have been associated with the early establishment of maturity. Secondary sex characters appeared fully developed, and the lower extremities appeared short in comparison to the trunk. In addition to this bodily proportion there were found distributions of fat such as are seen in the adult genital region and a large breast development. On measuring this patient carefully, however, with anthropometric instruments it was found that her lower extremity stature ratio was nearly 60, which is the ratio commonly found in the eunuchoidal type.

Figures 17 and 18, with the black line on the abdomen, show the level to which the crest of the ileum actually reaches. This character immediately changes the aspect of the case and sug-

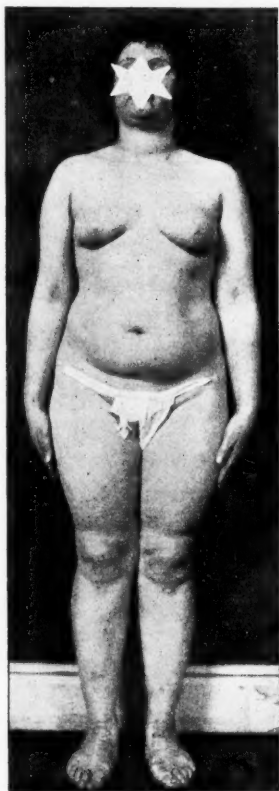


Fig. 16.



Fig. 17.—Case originally sent to clinic as showing the indications of sex precocity. Note the short lower extremities and long trunk.

gests a lowered or retarded sex development. Palpation of the breasts made it clear that there was practically no breast tissue present, but simply masses of fat.

In the Constitution Clinic at the Presbyterian Hospital we have measured a certain number of these fat children, and, on analyzing their measurements, two definite conclusions have



Fig. 18.



Fig. 19.—The same case as Fig. 18 with mark indicating actual position of pelvis, showing the eunuchoidal skeleton.

been arrived at. In the first place, skeletal measurements of children at present, for want of sufficient comparative data, are of doubtful value because of the growth factor. It is probably

not justifiable to compare children with a year or even six months' age difference as we would compare full grown adults belonging to a given disease group. The second observation arising from the measurements of these fat children is that so far as we have been able to correlate our measurements with the studies that have been made upon the size of children at different ages, these children have shown skeletal development coordinate with the accepted figures for their age. In other words, these fat children, as we have seen them at Presbyterian Hospital, have shown the average skeletal growth in proportion to their age, and their disturbance of form has been due entirely to excess fat deposition. All of our male cases have shown one of the two main indications of incomplete development of the gonads, namely, (1) small size of the testicles, or (2) the presence of a very marked degree of partial cryptorchidism.

The other great group of growth retardation disturbances is that of infantilism. One of the classical examples of this condition is that described by Lorain, in which there is complete arrest of development. Figure 20 was originally reported by Ettore Levi⁴ in 1908, and since then has been reported several times, among others by Cushing. The outstanding feature of the skeletons of this type of case, in addition to the fact of the small size, is the continuance of the open epiphyses. These

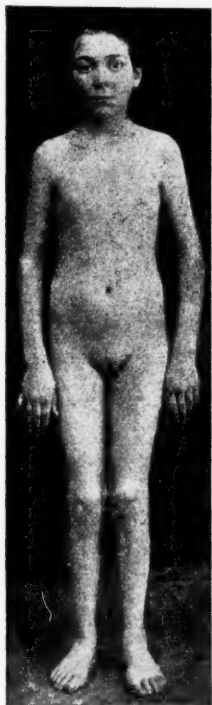


Fig. 20.—A case of the Lorain type, first observed by Ettore Levi in 1908. (Reproduced from Cushing.)

cases are also ascribed to disease of the pituitary gland. In this connection it is interesting to show the photographs of a case which was observed at the Rockefeller Institute Hospital in 1910. This patient (Fig. 21), aged ten and a half, was originally studied by Dr. Christian A. Herter as a case of intestinal in-



Fig. 21.—Case of intestinal infantilism of Herter which subsequently changed into the appearance of the Fröhlich type.



Fig. 22.—The same case as Fig. 21 one year after, when the change from the intestinal infantilism type to the Fröhlich type had taken place.

fantalism. The boy was not treated by any glandular extracts, but was simply given good care and nourishing food, and at the end of about a year he achieved the appearance seen in Fig. 22. Whatever the cause of the undernourished condition seen in Fig. 21 it was not due to the fact that the boy had not had every opportunity at home for the best nourishment and care. This

case left the hospital about a year after the second photograph was taken and did not reappear for four or five years. By that time he had grown to be a large, classical, fat Fröhlich type. He died suddenly of pneumonia.

One of the most extensive studies of the whole subject of infantilism is that by the Italian observer, Nicola Pende,⁵ which was made in 1912. He has called the condition general hypoevolutismus, and has divided this general deficiency according to the age of development which the particular case represents in its body form. Thus, he speaks of fetalismus, puerilismus, and juvenilismus. Figure 21, then, might well be classified as representing, if not the stage of fetalismus, one not far removed from it. Lehmann and Van Wart⁶ have also discussed this subject.

There is one other undetermined and interesting group of growth and development disturbances which has been ascribed to certain glandular pathology. This is the group which deals directly with underdevelopment and delayed development, or precocity and overdevelopment of the sex glands. A consideration of these various types of restraint or limitation of growth immediately raises the question of what the mechanism can be which stops the growth process at all. Is the mechanism which retards or checks growth so that the individuals remain undeveloped the same as that which stops growth when the individual finally attains his predestined full adult size and shape?

Figure 23, taken from Cushing, is of his Case XLVII which corresponded to the descriptions of sexual precocity which had been found in association with tumors of the pineal gland, but operation on this case failed to reveal any tumor either of the hypophysis or the pineal. Neurath⁷ also discussed a similar case. In connection with this case it is interesting to call attention to a case in the series of Cushing in which sexual precocity and hypertrichosis (in a girl) were associated with infantilism, uncinate fits, amenorrhea, and asthenia. This individual, aged nineteen, was undersized and childish, but no tumor could be found at operation.

Obviously, the explanation of all these conditions is far

from clear. Tumors of the pituitary have been found both with acromegaly and gigantism, as well as with infantilism of the Lorain type and adiposity and genital dystrophy of the Fröhlich type. Sex precocity in the male has been found with tumors of the pineal, and in Cushing's case without evidence of intracerebral tumor. Sexual precocity, with virilism and infantism in the female, has been found as reported by Cushing

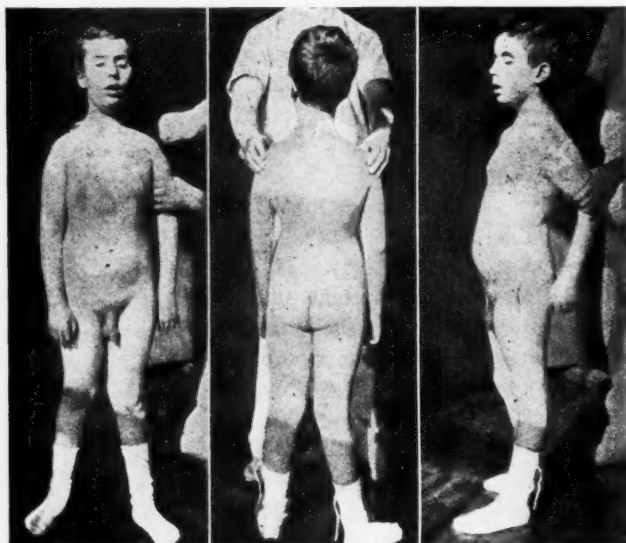


Fig. 23.—Case of precocious sexual adolescence, Cushing's Case XLVII, aged eight years.

without brain tumor. Virilism in the female has been found as described by Gallais⁸ in connection with bi'ateral tumors of the adrenal glands, and also associated with tumors of the ovaries, and possibly with tumors of the pituitary. Practically all of these conditions are seen in cases in which no glandular pathology can be demonstrated in life or found at autopsy.

For convenience in thinking about this confused mass of fact the following tables are presented. For again this ques-

tion arises: In the presence of so many different clinical expressions of similar glandular pathology can we assume that clinical syndromes which simulate the results of glandular pathology are due to faulty glandular balance? Animal experimentation has thrown much light on the subject of the function of the endocrine glands. Good clinical observations of the unusual case often almost corroborate the results of animal experimentation.

TABLE A

Pediatric period, 0-12-14 years.	{ Outstanding feature, growth	Rate	Pathologic acceleration	{ Glandular pathology
			Physiologic acceleration	{ Hereditary influence
			Physiologic retardation	{ Environment: (a) Nutrition (b) Infection
		Extent and what stops it (?)	Pathologic retardation and dispro- portions: (a) Psychic (b) Physical	{ Glandular pathology
			Dwarfism	{ Special parts
			Average Gigantism	{ Bony Soft parts

TABLE B

Puberty period, 10-15-16 years.	{ Pathologically precocious Physiologically precocious	{ (tumor of pineal?) Hereditarial influences Environment: (a) Nutritional (b) Infectious (mumps)	
			Physiologically delayed
			Pathologically delayed
			{ Lorain Fröhlich } (Pituitary tumor?)

Two main questions arise for further discussion: Why does similar pathology of the glands produce different symptom complexes in different individuals, and what are the limits of the activities of the glands of internal secretions?

For example, in the so-called Fröhlich syndrome is the defect primarily in the pituitary, with a secondary genital fault, or vice versa? If the primary fault is in the pituitary and no tumor is present, then one is forced back upon the consideration of the hypothesis that there is a hereditarial fault in the quality of the pituitary tissue.

We are moving into an uncharted sea and it is necessary to proceed with the same respect for observed facts and their correlation that the mariner has under such conditions. We must heave the lead and be sure that it hits bottom, and then note the character of the sand or mud which adheres to it. We must also be sure that we do not mistake fog banks for hillsides. The advance into the territory of the endocrines in their relation to growth and development will depend upon the accuracy of clinical observation and the correctness of correlation when opportunities for pathologic and physiologic study of the unusual case present themselves. I believe that the most objective point of view in the study of constitution as we find it, without yielding to hypothetic explanation, is still in order, as it has always been since Hippocrates pointed the way, and that if careful objective study and correlation be carried out, the explanation of these most interesting faults in growth and development will become apparent.

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CLINIC OF DR. ROBERT L. LEVY

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CARDIAC PAIN

ITS CONSIDERATION FROM THE STANDPOINT OF NOSOLOGY

"THERE is one eminent instance in which an assemblage of symptoms is made to bear the name of a disease—*angina pectoris*." Thus wrote Latham in 1846. It is a curious fact that a descriptive term meaning, literally, "strangling in the chest," applied by Heberden in 1768 to a group of cases presenting "strong and peculiar symptoms," should have been perpetuated these many years by students of clinical medicine. A serious nosologic consideration of the matter is not merely "factitious hair splitting between symptom group and disease," as so distinguished an author as Sir Clifford Allbutt would have us believe. For looseness in classification makes for careless thinking; and careless thinking leads to inaccuracies in all forms of scientific procedure.

The outstanding feature of cases commonly called *angina pectoris* is paroxysmal pain in the chest. This may vary in severity, location, radiation, duration, and frequency. Now, pain or discomfort experienced in other parts of the body does not commonly suffice, merely because of its presence, to justify deductions as to its source of origin or the nature of its cause. Thus, pain in the right upper quadrant of the abdomen may be due to one of a number of disturbances in pathologic physiology, either in an organ in the immediate vicinity of the site of origin of the discomfort or referred from another more distant viscus. Certainly the character of the pain gives no exact clue as to the underlying pathologic state and affords no basis for affixing to it a descriptive term intended to indicate a distinct disease

entity. Consideration of the clinical condition as a whole serves to establish a more or less accurate diagnosis and furnishes indications as to prognosis and therapeutic management.

It is claimed by those desirous of retaining the term, either for sentimental or perhaps more profound reasons, that the symptomatology and course of the clinical picture are so clearly defined that they justify a specific designation. Yet how ludicrous has become the terminology of these enthusiasts! Recall, for example, true and false angina, pseudo-angina (Osler), primary and secondary angina (Mackenzie), major and minor angina (Allbutt), the mock anginas (Allbutt), angina vasomotoria (Nothnagel), and angina sine dolore. Truly an imposing array of terms for what we are asked to consider a "disease entity."

All students of the condition are unanimous in describing a variable pathology. All agree that there are differences in the character of the paroxysms. The *angor animi*, or fear of impending dissolution, upon which much emphasis has been placed, may or may not be present. The classical instances of Thomas Arnold and John Hunter furnish evidence that the patient may die in the first great anguish, as did the schoolmaster of Rugby, or, like Hunter, live to suffer for twenty years, "his life in the hands of any rascal who chose to annoy or tease him." Yet no real effort has been made to determine the reasons for these striking deviations from the hypothetic pattern.

The discussion is not merely one of academic terminology. Mere quibbling is unprofitable. The evil in employing a generic term to define paroxysmal attacks of pain in the chest lies in the fact that it has led practitioners of medicine to be content to give a name to a symptom which may be an expression of a variety of different disturbances in the domain of the cardiovascular system. It has discouraged efforts to make more exact diagnoses based upon a consideration of pathogenesis. And in the train of inaccurate diagnoses have followed false prognoses and harmful therapy. How frequent it is to see in the consulting room a patient and his family who have been terrorized because some thoughtless physician has told the *pater familias* that he has "angina pectoris." According to the usual lay point

of view they have pictured to themselves an individual suffering from a series of agonizing attacks, with sudden death overtaking the victim while walking in the street. What a relief to find that with suitable measures instituted to control the beginning heart failure associated with hypertension the paroxysms disappear and, under proper régime, do not recur. What a satisfaction to the young woman with attacks of precordial pain to know that she is not suffering from angina pectoris, but from a state of nervous exhaustion, of which the pain under the left breast is but one manifestation. What a therapeutic accomplishment for the man with syphilitic aortitis, who may be made comfortable by potassium iodid. How important for the man of affairs with coronary thrombosis to set his house in order while he may.

The mechanism by which cardiac pain is produced is as yet but imperfectly understood. The late Professor Huchard is said to have collected no less than 80 hypotheses on this subject. It may well be that it is not possible to explain all varieties of heart pain upon the basis of a single physiologic disturbance. Two concepts seem to me to be worthy of special consideration at the present time—the one championed by Sir James Mackenzie, the other by Sir Clifford Allbutt. The advocate of each of these theories, for as yet they may not be regarded as proved, aims to exclude the arguments of his adversaries on the basis of what the logicians would term “the desirability of a parsimony of hypotheses.”

Reduced to their simplest terms, these two hypotheses may be briefly stated. Mackenzie is of the opinion that when the heart muscle is obliged to contract under unfavorable circumstances, be these due to deficient blood-supply to the myocardium or the result of disease, afferent impulses are carried to the central nervous system, which are then referred to various parts of the surface of the body and give rise to painful impressions. The pain is an expression of myocardial exhaustion. In view of the fact that there are afferents from the vagus and sympathetic trunks, terminating at levels in the cord from the fifth cranial to the fourth thoracic segments, it is in the domain of the pe-

ripheral distribution of efferents from these levels that the pain is experienced. The areas to which the discomfort is commonly referred are the jaw, neck, anterior chest wall, and inner aspect of the arm, chiefly, though not exclusively, on the left side. Upon the sensitiveness of the individual's nervous system and upon the strength or quality of the stimulus at its point of origin depends the severity of the resulting pain.

Allbutt is inclined to regard cardiac pain as due to a lesion in the supracardiac aorta, which he calls the "anginiferous area." From this region the pain is referred, as has been described, to the realm of cutaneous sensibility. "This first portion seems to be the most sensitive, and the lesion may break into angina when it penetrates to a certain depth; down, as I suggest, to the outer fibrous investment of the vessel. In angina tension is probably the mechanism; and from this point of view we may regard the ascending aorta as the tendon of the heart."

But the problem which we have undertaken to discuss does not concern itself with a consideration of the underlying mechanisms. An attempt has been made to indicate the futility, and, indeed, the danger of endeavoring to group a series of cases having a prominent symptom in common, under one generic name. What, then, are the conditions with which cardiac pain is found to be associated? The following classification, though perhaps incomplete and subject to modification, has been found to furnish a practical working basis.

Classification of Cardiac Pain

(according to the clinical conditions with which it is associated)

1. Heart failure (myocardial exhaustion).
2. Hypertension.
3. Aortitis:
 - (a) Syphilitic,
 - (b) Arteriosclerotic,
 - (c) Rheumatic.
4. Aneurysm of the aorta:
 - (a) Syphilitic,
 - (b) Arteriosclerotic,
 - (c) Mycotic.
5. Rupture of the aorta.

6. Coronary artery disease:
 - (1) Stenosis:
 - (a) Syphilitic,
 - (b) Arteriosclerotic.
 - (2) Occlusion:
 - (a) Thrombotic,
 - (b) Embolic,
 - (c) Syphilitic,
 - (d) Arteriosclerotic.
7. Tobacco poisoning.
8. Pericarditis:
 - (a) Fibrinous,
 - (b) With effusion,
 - (c) Adhesive.
9. Cardiac neurosis.
10. Pathogenesis undetermined.

Precordial pain is a common complaint. Thus, of 100 consecutive patients seen in the consulting room, 24 mentioned pain in the region of the sternum or left breast either as the chief complaint or as one of several discomforts. According to the diagnoses made, the conditions with which the pain was associated were as follows:

Heart failure.....	8
Cardiac neurosis.....	6
Coronary artery disease.....	6
Aortitis.....	2
Aneurysm.....	1
Tobacco poisoning.....	1

It is surprising to find how infrequently it is necessary to index cases in the file labeled "cardiac pain—pathogenesis undetermined." Modern methods of clinical examination have made possible the more accurate translation of the phenomena observed at the bedside into terms of morphology and function. At the necropsy table the basis for the symptoms in cases hitherto obscure often becomes intelligible.

The chief characteristic of the group of cases classed as heart failure was the fact that the pain was related to such events as would tend to throw an added burden of work on the weakened heart muscle, such as physical effort, emotional stress, exposure

to cold, abdominal distention, unpleasant dreams. Rest in comfortable surroundings afforded relief. The cases with affections of the coronary arteries also logically might be placed in this category. Where the evidence warranted it seemed desirable, for purposes of more accurate classification, to place them under a separate heading, for these individuals often do not fare as well as others in whom fatigue symptoms are referable to other causes. Into the heart failure group fall many of the cases which the older clinicians would term "true angina." I shall cite briefly the history of one such patient presenting certain features of interest:

Mr. W. E., aged forty-five, stock broker, was first seen by me on March 14, 1923, complaining of precordial pain and paroxysms of irregular action of the heart. His father died at forty-five of acute cardiac failure. The patient had been an unusually healthy and vigorous man, participating actively in various forms of outdoor sport. He had two attacks of malaria, paratyphoid fever thirteen years before, and frequent attacks of tonsillitis as a child.

The present illness began two years before with acute tonsillitis. His physician, listening to his heart, noticed that it was irregular and diagnosed the arrhythmia as auricular fibrillation. The arrhythmia lasted only a few hours, and following the attack he did not modify his life in any way. From then on there occurred a succession of attacks of irregularity, each longer than its predecessor. They now lasted for as long as half a day. He had five attacks in the past three months. An electrocardiogram taken during a period of irregularity confirmed the diagnosis of auricular fibrillation.

Pain first appeared in the fall of 1921 with the onset of cold weather and was a more recent symptom than the fibrillation. It was definitely related to exertion, such as running upstairs or playing golf, and was also induced by walking while wearing a heavy overcoat. The pain was very severe and extended transversely rather than up and down. There was no radiation to the arms. The heart felt as though gripped in a vise and he was obliged to stop whatever he was doing. The discomfort then disappeared in about two minutes. At no time had there been dyspnea or swelling of the ankles.

Examination revealed a healthy looking man with no apparent discomfort. The retinal arteries were quite thin and tortuous. The heart was not enlarged, either by percussion or in the orthodiagram. The rhythm was regular; the rate 64 to the minute. The sounds were not vigorous, but there was no splitting of the first sound. At the apex a short systolic murmur was audible. The radials and brachials were distinctly thickened. The blood-pressure was 146/94. The urine and Wassermann were negative.

The electrocardiogram (Fig. 24) was of real value as giving evidence of an affection of the myocardium. It showed sinus rhythm, with a rate of 70. There was left ventricular preponderance. The form of the complexes and the wide Q. R. S. interval indicated intraventricular block, affecting the

right branch of the bundle of His. The P-R. (conduction) time was normal. Comparison of these curves with others made in September, 1921 and March, 1923 showed only minor points of difference. The defect in the right bundle branch had, therefore, been present for at least eighteen months.

During the year following this examination it was possible to control the attacks of fibrillation quite satisfactorily with small daily doses of quinidin. The pain, however, increased in severity and frequency. At the present

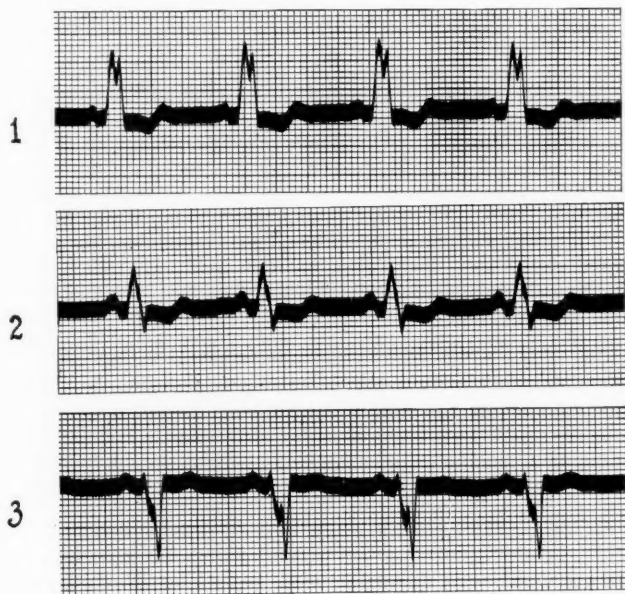


Fig. 24.—*Electrocardiogram of Mr. E.*: Sinus rhythm; rate 70; left ventricular preponderance; intraventricular block; Q. R. S. 0.11 to 0.12 second; P-R. 0.14 to 0.16 second; R-wave notched (Leads I and II); S-wave notched (Lead III); T-wave diphasic (Leads I and II).

time the patient still attends to his business each day, but has been obliged to lead a relatively quiet existence if he desires to remain comfortable.

Discussion.—The physical findings in this patient were certainly not sufficiently striking to arouse the suspicion of organic heart disease. It was from the history and the electrocardiogram that the serious nature of the trouble was revealed. Unquestionably, he is suffering from disease of the myocardium.

Whether this is due to focal inflammatory lesions or to coronary artery atherosclerosis it is not possible to say with certainty. In view of the arterial changes in both retinal and peripheral vessels, in spite of the comparative youth of the patient, I am inclined to believe that the muscular lesion rests on a vascular basis. Experience has shown that an electrocardiogram of this form is not infrequently found in patients with arterial disease of the heart.

Another important group comprises those individuals with discomforts referable to the heart, in whom no signs of organic heart disease are found and whose cardiac symptoms are but one expression of general nervous imbalance or fatigue. For want of a better term we call the condition a cardiac neurosis. In the series of 100 patients previously mentioned, 20 were so diagnosed. Of these 20, 6 complained of precordial pain. It is interesting to recall that Ernst Romberg, in his valuable treatise on the heart, states that about one-quarter of the patients in his private practice who consulted him because of cardiovascular disturbances were suffering from neuroses of the heart or blood-vessels. The following is a case in point:

Miss M., a spinster of twenty-seven, was first seen on September 27, 1922, complaining of pain in the region of the heart. She was born in the Middle West and had traveled widely. As a young girl she participated in the usual school activities. She spent two years at Columbia as a graduate student of music. In childhood she had typhoid, pneumonia, and growing pains.

The present illness began three years before. During the influenza epidemic she did social service work and was under considerable strain. At this time she first noticed that she became short of breath on going upstairs and shortly thereafter was distressed by sharp, shooting pain in the region of the left breast. This at first appeared only after exertion, but subsequently occurred at other times. It was sharply localized and did not radiate down the arm. She was examined by a physician, who told her that "her heart was dilated and the muscle was stretched out thin." He also told her that she had a leaky valve and advised her to go to bed for three months. From this time on she was a confirmed cardiac invalid. She rested for five months, was put on a restricted diet, and was thoroughly unhappy. During the following three years she undertook various forms of activity to occupy her time, both in this country and abroad. There was pain at times and dyspnea on exertion. With rest and quiet the symptoms always abated, though never disappearing completely. She was able to take short walks of half an hour at a time. She slept poorly.

Examination showed a sallow, undernourished young woman, not altogether unattractive. She was much concerned about herself. Save for a late short systolic murmur at the apex, the heart, as well as the other systems of the body, were quite negative. Orthodiagram, electrocardiogram, vital capacity, and the exercise test (hopping on one foot) were normal.

The patient was assured that she was not suffering from organic heart disease. Gradual resumption of full activity was advocated and plans were made for occupying her time. The diet was outlined with a view to insuring a gain in weight. Improvement was rapid, and with the gradual disappearance of symptoms confidence increased. On November 17th, about two months later, the patient reported that in her rounds of social service work she had walked up six flights of stairs without discomfort.

Discussion.—It is desirable, when possible, to look beneath the surface for the causes of the mental maladjustments which result in the somatic symptoms characterizing a neurosis of this sort. In the course of a few weeks this girl, with a burst of tears, poured out her story. She had never been attractive to men. Her friends and sisters, after the usual rounds of social activity, had one by one gotten married. Although passionately fond of children, she saw no prospect of having a home and a family of her own. Between herself and her parents there existed no bonds of sympathy. She had one love affair, culminating in an engagement, which was broken off because her fiancé was found unworthy of her affection. She sought an outlet in the field of social service, but found it unsatisfactory. And to cap the climax, her physician had told her that she was suffering from chronic heart disease.

She no longer complains of precordial pain and dyspnea. She has formulated a philosophy of life which is fairly satisfactory. I trust, for her sake, that she may one day find a good husband.

SUMMARY

Arguments have been adduced in an attempt to show that the employment of the term "angina pectoris" as a generic name for a group of conditions associated with cardiac pain tends to make for inaccurate diagnosis from the standpoint of pathogenesis. It is suggested that this terminology be abandoned, and that pain be regarded as a symptom of the various

pathologic states in which it is found. There has been presented a practical classification of the clinical conditions with which cardiac pain is found to be associated. By careful analysis of such cases data may be accumulated which will enable patients suffering from these conditions to receive more appropriate therapy, and by studying the life-history of many such individuals more precise prognostic criteria may be developed.

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NOTES ON THE TREATMENT OF DIABETES MELLITUS

1. A Simplified Weighed Diet.
2. The Use of Insulin.

1. **A Simplified Weighed Diet.**—The proper management of cases of diabetes whose starch tolerance is moderately or markedly impaired demands that weighed diets be used exclusively. Both in hospitals and private practice this is often accomplished only with considerable effort. The actual weighing of the food gives no trouble; the greater difficulty lies in the calculation of the food ingredients necessary to make up the quantities of protein, fat, and carbohydrate called for in the dietetic prescription. It is believed that the scheme to be detailed subsequently will do away with some of the objections to weighed diets; for the past six months this food list has been used with much satisfaction in hospital, dispensary, and office practice.

It is proper in the first place to mention the reasons for the given proportion of fat, carbohydrate, and protein in the present plan. Similar outlines could, of course, be made with other proportions of the food materials so as to meet the theoretic demands of individual physicians.

The amount of protein prescribed has been about 1 gram per kilo. We have failed to obtain satisfactory nitrogen balances with the lower ration of $\frac{2}{3}$ gram per kilo which is being so generally resorted to at the present time.

The quantity of fat must be adjusted to the amount of starch consumed. Fatty acid and glucose are derived from the food as follows:

	Glucose, grams.	Fatty acid, grams.
100 grams protein in the body yield.....	58	46
100 grams fat in the body yield.....	10	90
100 grams carbohydrate in the body yield.....	100	0

When less than a certain proportion of glucose to fatty acid is metabolized some of the fatty acids are not changed to carbon dioxid and water, but remain unoxidized, the so-called acetone substances appear in the urine, may accumulate in the body, and thus bring about an acidosis. There has been much debate as to the exact fatty acid—glucose ratio (or the F. A. : G.)—that will result in ketosis. The careful work of H. B. Richardson and W. S. Ladd¹ bears out the earlier observations of Woodyatt and Shaffer that the maximal F. A. : G. ration without the occurrence of ketosis is about 1.5 : 1. The high fat diets now in vogue, with much higher F. A. : G. ratios can apparently be administered in some cases without the production of an acidosis because the extent of the ketosis, according to Richardson and Ladd, varies with the actual food oxidized, and not with the diet; safety in the use of high fat diets depends, according to these observers, on the ability of the patient to contribute carbohydrate from his own tissues and to store fat. In our experience we have frequently encountered severe acidosis in patients in whom a diet with a F. A. : G. ratio higher than 1.5 : 1 has been given for a few weeks. In the present diets, therefore, a somewhat lower ratio has been resorted to. Thus calculating the F. A. : G. ratio in diabetic diet No. 5 we have:

	Fatty acid, grams.	Glucose, grams.
75 grams protein yield.....	34.5	43.5
175 grams fat yield.....	157.5	17.5
100 grams carbohydrate yield.....	0	100
	192.0	161.0

$$\frac{\text{F. A.}}{\text{G.}} = \frac{192}{161} = \frac{1.2}{1} = 1.2$$

This ratio of 1.2 : 1 is the same in all the "diabetic diets"; it is well within the limits of safety and gives a palatable proportion of fats.

¹ Richardson, H. B., and Ladd, W. S., Jour. Biol. Chem., 1924, lviii, 931.

The carbohydrates are not cut to the minimum in these diets. In the long run food without some starch becomes irksome and makes eating a burden to the most abstemious individual; now that we are fortunate enough to have insulin as a therapeutic agent it is no longer necessary to be as insistent on starch restriction as formerly.

The total caloric requirement may be calculated in various ways; from the clinical point of view we have found that diet No. 4 (1876 calories) is usually ample for smaller persons and No. 5 (2345 calories) for larger individuals. When higher diets can be taken by the patient it is generally unnecessary to weigh the food.

The acidosis diets on the chart (page 84) are for emergencies when a very low fat régime is indicated; for routine use the diabetic diets are to be used.

2. The Use of Insulin.—The work initiated by F. G. Banting has succeeded in furnishing us with "insulin," an extract derived from the islands of Langerhans of the pancreas, which, on hypodermic injection, has proved to be capable of controlling the deranged metabolism of diabetes mellitus. The value of this scientific contribution to clinical medicine is inestimable; when dietetic treatment fails to control this disease the proper use of insulin will restore the normal functions and apparently prolong life indefinitely.

In a general way the mode of using insulin is known; the details of its administration are not so generally appreciated and it is proposed to mention a few cases that illustrate some salient points.

The preparation of insulin used in the United States is that distributed as "letin." This is made up in three strengths—U 10, U 20, and U 40—put up in 5-c.c. vials with rubber caps for hypodermic use. The figures 10, 20, and 40 indicate the number of units contained in each cubic centimeter of the preparation. The first products put out were designated as H 10 and H 20. The H unit was the amount of insulin required to lower the blood-sugar of a 2-kilogram rabbit below 0.045 per cent., resulting in convulsions within two to five hours. The

TABLE 1

(This chart when printed on light cardboard and folded once furnishes a convenient diet card; it is self-explanatory.)

DIET IN GRAMS										Vegetables 10% CH 10% Fat	Vegetables 10% CH 10% Fat	Fruit 10% CH 10% Fat	Meat and Fish 20% CH 20% Fat	Butter 10% CH 10% Fat	Cream 20% 10% CH 10% Fat	Eggs 10% CH 10% Fat	Olive oil 10% CH 10% Fat	Bacon cooked 10% CH 10% Fat	Milk 10% CH 10% Fat	Skimmed milk 10% CH 10% Fat	Gelatin 10% CH 10% Fat	Fruit 20% CH 20% Fat
Diabetic Diet	CH	Prot	Fat	Cal	Meals																	
1	20	15	35	469	Breakfast	200						70			30							
					Lunch Supper	200							45	12								
2	40	30	70	938	Breakfast	100	90			100	100			15	60							
					Lunch Supper	200						100		15								
3	60	45	105	1407	Breakfast	100	90			100	100			15	60							
					Lunch Supper	200								15	30	50	30					
4	80	60	140	1876	Breakfast	100				100	100			20	60	50		30				
					Lunch Supper	100				100				20	30		15	30				
5	100	75	175	2345	Breakfast	100				100	100			30	60	50		30				
					Lunch Supper	100				100				30	30		15	30		200		
Acidosis Diet 1	20	30	4	242	Breakfast	100									100						100	
					Lunch Supper	100															100	
2	60	45	5	477	Breakfast	100					100										100	
					Lunch Supper	100					120										100	
3	100	65	5	723	Breakfast	100					100										200	100
					Lunch Supper	100				100											200	80

Foods without food value as desired with any diet.

Vegetables and Fruits 3% CH, 1% prot	Vegetables, Fruits and Cereals 10% CH, 1% prot	Vegetables, Fruits and Cereals 20% CH, 3% prot	Meat and Fish 20% prot, 20% fat	Fish 20% prot, 3% fat	Foods Without Food Value
Artichokes canned	Beets	Artichokes fresh	Beef boiled	Bass black	May Be Taken As Desired
Asparagus	Carrots	Beans baked	Beef corned	Bass sea	Agar agar
Beans string	Dandelion greens	Beans baked canned	Beef kidney	Bass striped	Broth skimmed
Beans wax	Green peas canned	Corn green	Beef roast	Blue fish	Clear coffee
Beet greens	Horseradish	Corn green canned	Beef steak	Cod fish fresh	Clear tea
Brussels sprouts	Okra	Green peas fresh	Beef tongue	Cod fish salt	Cocoa shells
Cabbage	Olives green	Lima beans	Capon	Flounder	Cracked cocoa
Cauliflower	Onions	Macaroni cooked	Chicken broilers	Haddock	Mineral oil
Celery	Parsnips	Potatoes	Chicken fowl	Hallibut	Starch free bran
Cucumbers	Pumpkin	Rice boiled	Duck	Perch yellow	biscuits
Endive	Squash		Goose	Pollock	Starch free bran cereal
Kohlrabi	Turnip		Guinea Hen	Porgy	Thrice boiled vegetables
Leeks	Apples	Apricots	Ham	Shad roe	
Lettuce	Blackberries	Bananas	Lamb chops	Smelt	
Marrow	Cranberries	Blueberries	Lamb roast	Trout	
Mushrooms	Currants	Cherries	Mutton chop	Weak fish	
Olives ripe	Gooseberries	Huckleberries	Mutton	White fish	
Pickles	Grapefruit edible part	Nectarines	Pork chop		
Radishes	Lemons	Pears	Pork roast		
Sauerkraut	Muskmelon	Plums	Squab		
Sorrel	Oranges	Hominy cooked	Turkey		
Spinach	Peaches		Butter fish		
Swiss chard	Pineapple		Eels		
Tomatoes	Raspberries		Halibut smoked		
Water cress	Strawberries		Herring smoked		
Rhubarb	Watermelon		Mackerel fresh		
			Mackerel salt		
			Salmon canned		
			Salmon fresh		
			Sardines canned		
			Shad		

Weight equivalents:

30 grams = 1 ounce

1 egg weighs 50 grams

Household measures:

1 flat teaspoonful = 5 grams

1 flat tablespoonful = 15 grams

1 heaping tablespoonful, cut meat

or fish = 30 grams

1 water glass full = 250 grams

present U units are 40 per cent. stronger than the original H units.

Insulin is effective only when given by hypodermic or intra-

venous injection. Except in emergencies the hypodermic method only should be used. The extract should be injected well into the subcutaneous tissues, not near the skin and not into the muscles. The site of the injections should be varied as much as possible so as to avoid the induration which is prone to occur; for the same reason it is advisable to use the most concentrated form of iletin feasible; an injection of $\frac{1}{4}$ c.c. is less likely to give trouble than 1 c.c.; whereas temporary induration and slight tenderness is a common sequel, abscesses are extremely rare, even when the patients inject themselves. The number of daily injections, the time of administration, and the size of the dose to be used are problems that demand the closest study of the effects of insulin in general, and a careful, painstaking scrutiny of the individual case as well.

The general effect of insulin is to lower the blood-sugar and diminish the sugar in the urine; at the same time the acidosis is lessened as shown by the increase of the carbon dioxid combining power of the blood and the falling off of the acetone bodies in the blood and in the urine. This is shown in Table 2 (page 86). In this case 23 units of iletin given hypodermically resulted in a drop of the blood-sugar from 0.308 to 0.150 per cent.; the greatest depression of the blood-sugar occurred in four hours, after which it again began to rise; the glycosuria ceased; the CO_2 combining power of the blood rose from 46 to a normal of 61; the acetonuria disappeared, and the acetone bodies in the blood were very much diminished.

This experiment (Table 2) shows that:

1. Insulin increases the utilization of glucose in the diabetic.
2. Secondary to the increased catabolism of sugar is the oxidation of fatty acids and, consequently, the disappearance of the ketosis and acidosis.

From observations made in a number of researches we know that:

3. Insulin, besides aiding the oxidation of glucose, causes it to disappear from the blood by furthering the processes which store the glucose as glycogen in the liver and probably in other tissues.

TABLE 2

Effect of Iletin on the Blood-sugar and Acidosis in Diabetes Mellitus

Male—Diabetes mellitus.

Time.	Iletin.	Blood.			Time.	Urine.	
		Sugar, per cent.	CO ₂ combining power.	Acetone bodies, mg.		Sugar, gm.	Acetone bodies, gm.
9.00	23 un.	.308	46	33	7.48	5.7	1.25
10.00					8.48	1.1	0.27
11.05		.256	52	32	10.30	2.5	0.44
12.05		.220	58	13	11.30	0.6	0.10
1.06		.180	61	3	12.28	0.1	0.02
2.12		.150	60	14	1.30	0.0	0.03
3.05		.172	60	14	2.30	0.0	0.02
4.03		.190	58	15	3.30	0.0	0.03
5.03		.181	55	17	4.30	0.0	0.04
					5.28	0.0	0.04

It is of importance from the clinical point of view to know what 1 unit of insulin will accomplish. Such general principles are subject to many exceptions, and it is absolutely necessary to treat each case individually and adjust the amount and frequency of insulin dosage to the metabolic peculiarities, the daily habits, and the economic status of every patient.

The effect of each dose of insulin is transient; our experience has been that, as measured by the drop in blood-sugar, it attains its *maximun in about four hours* (Table 2), and then gradually ceases to control the sugar metabolism. Whereas this may be regarded as the average, it varies much; thus in Table 3 the greatest drop in the glycemia occurs in eight hours. *The acidosis as measured by the CO₂ combining power of the blood is diminished, as might be expected, in direct proportion to the glucose utilized.* The setting aside of the acidosis is remarkable in its speed and thoroughness; the influence of insulin in this regard is sometimes, though not always, more rapid and more complete than the control of the blood-sugar (Table 2). We have found that *1 unit of insulin will cause a drop of approximately 8 mg. per 100 c.c. of blood.* This is well shown in Tables 2 and 3. This reduction of

TABLE 3

Effect of 30 H Units of Iletin on the Sugar and Carbon Dioxid Combining Power of the Blood

Male—Diabetes mellitus. Age twenty-five. 3/8/22.

Time.	Iletin.	Blood.		
		Sugar, per cent.	CO ₂ , vol. per cent.	
8.30 A. M.	30 un.	.342	30.1	Fasting throughout.
9.15 A. M.				
11.15 A. M.		.197	35.7	
1.15 P. M.		.180	38.5	
3.15 P. M.		.131	40.4	
5.15 P. M.		.104	44.0	
12.30 A. M.		.255	36.6	

the blood-sugar is really the action of starvation plus the effect of insulin. That the insulin exerts considerable effect beyond that brought about by starvation may be noted in Table 4 (page 88). Two other very important facts must be kept in mind when comparing the effects of insulin and starvation in the diabetic organism. These are, in the first place, that *insulin diminishes the blood-sugar and sets aside glycosuria because it brings about an increased utilization of glucose, whereas, according to the quoted paper of Richardson and Ladd, starvation accomplishes this by allowing the accumulated glucose to escape in the urine*; in one case the stranded ship is floated off the sand-bar by the rising tide with its freight intact, while in the other the cargo has to be thrown overboard to enable the vessel to proceed on its way. The second point for consideration is that *insulin brings about a storage of glycogen from glucose*; the importance of this process is not thoroughly understood; that a reserve food supply is furnished the body is perfectly obvious; it may be that glycogen aids in the retention of fluid in the desiccated diabetic; it may have far-reaching influences that we can only speculate about for the moment; such a storage of glycogen certainly does no harm, and to bring it about it may be very worth while to administer a single small daily dose of insulin to many diabetics

TABLE 4

Time.	Case I.		Case II.		Case III.	
	Blood.		Blood.		Blood.	
	Sugar, per cent.	CO ₂ com- bining power.	Sugar, per cent.	CO ₂ com- bining power.	Sugar, per cent.	CO ₂ com- bining power.
9 A. M.	.220	50	.315	61	.280	25
1 P. M.	.220	49	.272	66	.236	32
5 P. M.	.140	62	.263	63	.234	35
Change in 8 hours.	— .080	+12	—52	+2	—46	+10

Spontaneous changes in the blood-sugar and plasma CO₂ which occurred in diabetic patients in an eight-hour period. These patients received water only, no food was taken, and no medication administered for fifteen hours before and during the observation.

Time.	Blood.			Blood.			Blood.		
	Sugar, per cent.	CO ₂ com- bining power.	Iletin, units.	Sugar, per cent.	CO ₂ com- bining power.	Iletin, units.	Sugar, per cent.	CO ₂ com- bining power.	Iletin, units.
8.15	.200	33	5	.319	58	20	.260	44	15
11.40									
1.40	.110	54		.250	69		.192	58	
3.40	.086	47		.197	70		.166	56	
5.40	.091	46		.208	65		.187	56	
7.40	.101	46		.220	65		.192	49	
9.40	.119	45		.238	64		.195	48	
Change with Iletin	—114	+21		—122	+12		—94	+14	
Spontaneous change	—80	+12		—52	+2		—46	+10	

Effects of Iletin in the same cases. The spontaneous changes are less marked in the blood-sugar and plasma CO₂ than those after Iletin. The transient action of the Iletin should be noted.

whose glucose tolerance is satisfactory and whose general hygienic state is not. Five to 10 units in the morning before breakfast has accomplished much for many such patients.

TABLE 5

M. Male, aged sixty-five. Diabetes mellitus.

Date.	Urine twenty-four hours.			Diet.				Iletin.	
	C. c.	Glucose.		CH.	Prot.	Fat	Cal.	Doses.	Total units.
		Per cent.	Gm.						
Dec.									
20	1250	1.0	12.5	80	60	140	1876	0	0
21	1396	.8	11.0	80	60	140	1876	2	10
22	580	1.2	7.0	80	60	140	1876	2	15
23	80	60	140	1876	2	20
24	670	1.5	10.1	80	60	140	1876	2	20
25	80	60	140	1876	2	30
26	690	2.0	13.8	80	60	140	1876	2	40
27	670	1.8	12.1	80	60	140	1876	2	40
28	1030	.6	6.2	80	60	140	1876	2	40
29	1020	.6	6.1	80	60	140	1876	3	45
30	500	.5	2.5	80	60	140	1876	3	50
31	1060	.2	2.1	80	60	140	1876	3	60
Jan.									
1	1290	.5	6.5	80	60	140	1876	3	60
2	700	.6	4.2	80	60	140	1876	3	60
3	1375	.1	.1	80	60	140	1876	3	60
4	1480	0	0	20	15	35	469	0	0
5	1420	0	0	20	15	35	469	0	0
6	1010	0	0	80	60	140	1876	0	0
7	1780	.4	7.1	80	60	140	1876	0	0
8	570	1.7	9.7	80	60	140	1876	0	0
9	960	0	0	80	60	140	1876	2	40
10	1440	0	0	80	60	140	1876	2	40
11	1980	0	0	80	60	140	1876	2	40
12	1000	0	0	80	60	140	1876	2	40
13	1560	0	0	80	60	140	1876	1	20
14	2030	0	0	80	60	140	1876	2	40
15	1110	0	0	80	60	140	1876	2	40

Case of diabetes mellitus treated with insulin; there is very little response to the insulin from December 20th to January 3d, even though comparatively large doses are used; a low diet for two days, January 4th and 5th, promptly does away with the glycosuria, which returns when the higher diet is resumed; *after the low diet, January 9th to 15th, the insulin becomes effective in rendering the urine sugar free, whereas it did not accomplish this before.*

From what has been said it must not be taken for granted that a low diet has no value in carrying out insulin therapy.

There are a few patients in whom this pancreatic extract has little or no effect. This is notably true in those diabetics complicated by arteriosclerosis or infections; in one such case we have seen 150 units a day administered without producing any diminution of the urinary or blood-sugar. In some patients the use of a low diet for several days will apparently "activate" the insulin. Thus in Table 5 (page 89) the glucose utilization shows very little response from December 20th to January 3d, though doses as high as 60 units per day are employed; a low diet for two days, January 4th and 5th, alters the situation so that the same diet which 60 units of insulin failed to digest we now find is consumed by 40 units so thoroughly that no sugar escapes in the urine. *Thus a temporary restriction of food in some unknown manner activates the insulin*; this we have found to be true in a number of cases; it is a very helpful procedure in many instances when the insulin is inert or sluggish in its action.

There are some facts that are very worth while noting in regard to the control of the acidosis in diabetes through the agency of insulin; they are well illustrated in Table 2. The control of the acidosis is "complete": there is an increased consumption of glucose; the CO_2 combining capacity of the blood returns to normal, the ketosis in the urine is set aside, and this is not due to retention of the acid bodies, characteristic of diabetes, in the circulation, for the ketosis of the blood diminishes at the same time. It may therefore be assumed that insulin brings about a normal oxidation of both glucose and fatty acids within the organism.

We have seen that 1 unit of iletin reduces the blood-sugar approximately 8 mg. per 100 c.c. Another method of gaging the dosage of iletin is the amount of starch which one unit will digest. There is a very great variation of the effect of the extract in this regard; it has already been mentioned that in some instances no carbohydrate whatsoever is consumed, in others as high as 20 gm. per unit has been noted. A fair average in our experience has been a utilization of 1.5 to 2.0 gm. of glucose for each unit of iletin administered. Table 6 gives the observations on this point in a case of diabetes mellitus of maximal

TABLE 6

C. Male, aged forty-four. Diabetes mellitus.

Date.	Urine glucose, gm.	Blood- sugar, per cent.	Iletin.		Carbo- hydrate utilized per unit iletin.	Weight, pounds.	Remarks.
			Doses.	Total units.			
1922							
Aug. 9	71.0			0		96	Diet contains about 1000 cal. Appears moribund. Iletin for one week. Diet about 2000 calories. Much improved.
28	108.6	.430		0		99	
Sept. 14	149.9	.333	1	10	?	109	
Nov. 2	13.3	.333	3	30	?	111	
15	0.0	.200	2	36	?	112	
1923							
Jan. 4	47.3	.312	2	50	?	119	H units replace U units.
March 14	24.9	.400	2	40	?	126	
April 10	50.5		2	40	1.9	126	
20	18.5		2	40	2.6	128	
May 7	32.0	.357	2	40	2.3	127	
15	99.8		2	40	0.6	123	
25	54.3		2	40	1.8	126	
June 5	61.3		2	40	1.6	124	
18	37.5	.285	2	40	2.2	129	
29	56.8		2	40	1.7	129	
July 6	55.0		2	40	1.8	123	
11	45.0		2	40	2.0	126	
16	26.6		2	50	2.0	127	
25	53.3		2	50	1.3	129	
Aug. 3	30.0		2	60	1.6	130	
Sept. 7	40.0	.322	2	60	1.4	134	
17	32.7		2	60	1.4	131	
26	12.0		2	60	1.9	132	
Oct. 1	20.4		2	40	2.9	132	
18	25.0		2	60	1.8	129	
22	26.0		2	60	1.9	128	
26	26.0		2	40	2.7	128	
Nov. 2	56.3		2	44	1.8	129	
15	33.3	.370	2	60	1.6	131	
28	53.0		2	50	1.4	132	
Dec. 12	14.1	.344	3	60	2.0	134	
21	15.1		3	60	1.9	135	
1924							
Jan. 11	21.9		3	65	1.4	137	
21	42.3		2	60	1.5	137	
28	32.5		2	60	1.5	139	
Feb. 14	65.0	.285	2	60	1.1	138	
March 13	11.6	.100	2	60	2.0	142	

Data from a case of very severe diabetes mellitus. Note the comparatively narrow range of the amount of carbohydrate utilized per unit of iletin; the improvement (judged by weight increase in the table) occurring in the presence of glycosuria and a hyperglycemia.

severity. The patient has been carefully studied, and he is, as far as can be determined, incapable of digesting glucose from any source, protein, carbohydrate, or fat; hence in him it is a comparatively easy matter to determine with fair accuracy the amount of starch which one unit of iletin will account for (Table 6).

In a general way it is seen that about 1.5 to 2.0 gm. of starch are handled per iletin unit. This constant degree of glucose utilization in this patient as compared to others is due to a number of conditions:

1. The study of the case indicates that the islands of Langerhans are completely destroyed and are not subject to functional recuperation or depression such as frequently occurs.

2. There have been no complications, especially infectious, which often have the tendency to lessen the potency of insulin.

3. This patient has a very stable nervous system; nothing disturbs his wonderful calm judgment and self-restraint; just before the use of iletin was begun in August, 1922 this man was moribund and, in spite of it all, unruffled as ever.

It is rare to find such a patient as a means of testing out the power of insulin units; it is well known that the functional power of the pancreas apparently grows stronger or weaker often as the result of proper dietetic treatment or of dietetic abuse or because of other reasons that frequently cannot be fathomed; nervous strain in many individuals lessens the ability of the body to digest sugar, such nervous tension may have a trivial cause, for instance, the necessity of rearranging the plans for an evening's entertainment, or it may be the reaction to a severe nervous shock; on the other hand, some persons, as the present case, seem to be immune to the effects of this world's worries; any infectious process, whether it be coryza, bronchitis, or enteritis, or more severe, as pneumonia or a purulent infection, boil, carbuncle, or infected gangrene, will have the tendency to lower the inherent strength of insulin. It is really necessary to bear these facts in mind when directing the use of this material, for any of the untoward incidents mentioned above, whether functional or anatomic, may necessitate an urgent change in the dosage. The far-reaching effect of these influences, which are of such constant occurrence in the daily existence of all of us, makes it evident that *to speak of the average capacity of the unit of iletin to digest a given amount of starch is impracticable*; in most instances it must be conceded that this is true; however, I believe *if these extraneous effects could be eliminated and the*

undisturbed damaged carbohydrate metabolism of the diabetic could be brought under the influence of insulin, that then 1 unit of insulin would digest about 2 grams of glucose. This is not a scheme of theoretic interest only, but it has a real practical value in two directions: first, it enables us to gage the proper dose of insulin to a certain extent if the urinary sugar excretion only is known; second, if iletin is not as powerful in its action as theory demands it may point to the necessity of looking for other elements in the case that may be remedied or improved by proper treatment.

In the administration of insulin it is often found that a smaller dose of the extract will bring about a greater digestion of starchy food per unit of iletin than larger doses. Thus in Table 6 on October 1st and 26th with the use of 40 units per day the amount of glucose utilized per unit of iletin is 2.9 and 2.7 gm., whereas when 60 units were given in the twenty-four hours the consumption of carbohydrate per unit was decidedly less. In studying Table 6 it is evident that there are exceptions to the above statement; however, in general we have found it to hold true; from the economic and therapeutic standpoint this fact is of considerable aid; it may account for the very good results some clinicians have achieved with small doses as compared to others who have resorted to much greater quantities without a proportionately better result.

The practical application of the above observation may be seen in Table 7 (page 94); the idea that smaller doses of insulin were more effective than massive ones was applied by using four doses a day instead of two. When treatment was begun with this child it was our intention to confine the insulin administrations to two doses a day, increasing them until the situation would be under control. We were soon disillusioned, for large amounts of iletin up to 120 units per day failed to check the glycosuria, and it was only when four injections were given in the twenty-four hours (the first as early after waking as possible, the last before going to sleep, and the two others at evenly spaced intervals during the day) that sugar ceased to appear in the urine; the most remarkable feature of the situation is that with

four doses a day 40 units could control the carbohydrate metabolism, whereas with fewer injections even 120 units did not, in spite of the fact that evidently, as judged by the presence of hypoglycemic shock, the limit of insulin administration had been reached. For details and clearer demonstration of these procedures the reader is referred to the legend and remarks of Table 7.

TABLE 7

Date.	Urine, glucose, gm.	Iletin.		Diet.				Remarks.
		Doses.	Total units.	Prot.	Fat.	CH.	Calories.	
Sept. 9	65	0	0	52	109	51	1436	The degree of glycosuria shows this to be a severe case.
Oct. 25	50	2	60	60	140	80	1867	Unsatisfactory effect of 60 units of iletin in two doses.
Nov. 5	59	2	80	60	140	80	1867	No noticeable difference when 80 units of iletin in two doses are used.
" 9	12	3	120	60	140	80	1867	Hypoglycemic shock on the next day with the same dosage of iletin; evidently the blood-sugar varies enormously with these doses because of the persistence of glycosuria and occurrence of hypoglycemic shock on the same day.
" 21	12	3	75	60	140	80	1867	Better control of glycosuria with three doses of iletin than with two (see Nov. 5).
" 30	10	3	50	60	140	80	1867	The frequency of dosage of iletin is more efficacious in controlling the glycosuria than the actual quantity injected.
Jan. 12	0	4	40	60	140	80	1867	

Extracts from the data of J. B., aged ten, severe diabetes mellitus; after various experiments it was found that *small, frequently repeated doses of iletin were of greater value in controlling the glycosuria than much larger doses given at longer intervals*; in fact, the frequency of dosage appeared to be of greater importance in this case than the number of units given.

The Frequency and Size of Insulin Dosage.—Insulin is usually administered just before meals. The object is to have the insulin act upon the hyperglycemia following each meal and also to prevent a hypoglycemic reaction which might occur if the insulin administration were not followed by food.

The number of doses of insulin per day may be one, two,

three, or four. A single large dose may be given, usually before breakfast, but in any event immediately preceding the meal containing the greater portion of the protein and carbohydrate of the day's food.

When the food is evenly or fairly evenly distributed throughout the day, two or three injections may be used. This is the procedure that is carried out in most cases at the present time. From what has been previously said it is probable that the effect of any one insulin treatment is terminated in about eight hours; it is therefore advisable, if the blood-sugar is to be controlled throughout the twenty-four hours, to give at least two injections.

TABLE 8

Male. Diabetes mellitus.

Time.	letin.	B. S.	letin.	B. S.	letin.	B. S.
7.00 A. M.	30 un.		15 un.		10 un.	
7.30 "	Breakfast.					
10.00 "		.266		.272		.284
11.45 "	0				10 un.	
12.15 P. M.	Lunch.		0			
3.00 "		.272		.274		.312
4.45 "	0		15 un.		10 un.	
5.15 "	Supper.					
7.00 "		.312		.274		.284

Diet—same on each day. *Effect of one, two, or three doses of insulin a day on the blood-sugar (B. S.).*

In Table 8 it is shown how the blood-sugar rises during the day when a single dose of insulin is administered, whereas it remains fairly constant either with two or three administrations. Since the comfort of the patient demands as few injections as possible, two in this patient, as in most, would be the choice.

It must be remembered that to obtain the best results the frequency of insulin dosage may have to be varied in the individual cases for many reasons. No iron-clad procedure in this respect should be followed by any physician or institution. The size of the dose of insulin requires a great deal of experi-

mentation for proper adjustment to the patient's needs. The necessity and the effectiveness of four doses a day, for instance, in the case shown in Table 7 has been discussed.

In the first place, a small dose (1 to 5 units) should be given on two or three occasions to determine whether the material produces toxic effects, or whether the patient is particularly susceptible to hypoglycemic shock. If neither of these conditions exist, 1 unit of insulin may be ordered per day for every 3 or 4 grams of glucose present in the twenty-four-hour urine; or one unit may be given for every 12 milligrams it is desired to reduce the blood-sugar during the day. (This, of course, supposes that the patient is being kept upon a diet constant in weight and in the proportion of fat, protein, and carbohydrate.) Subsequently the insulin is increased or diminished as the glucose of the blood and urine indicate; the ultimate object is to have the urine sugar free, the blood-sugar at a normal level, and enough food to furnish maintenance without undue gain in weight.

The necessity of close control of the patient so as to adjust the dosage of insulin to the needs of the moment cannot be too strongly emphasized. Table 9 furnishes the results in an extremely favorable case in which the sugar tolerance was markedly raised in a short period; this is an ideal achievement. The diabetic of Table 9 shows an amazing increase of tolerance for glucose with the use of insulin; whereas it required 45 units ofletin to maintain a sugar-free urine on December 18th, a sugar-free urine and a normal blood-sugar were obtained on January 30th without insulin while the patient was on the same diet.

In some instances it is dangerous to advise the use of insulin even though glycosuria exists. This is true when the blood-sugar is near a normal level in spite of the fact that sugar is being excreted in the urine. That there is danger of hypoglycemic shock under these circumstances is perfectly obvious. This state of affairs is especially frequent in children. Examples are given in Table 10 (page 98).

It is perfectly obvious that nearly every case of diabetes can be maintained with a sugar-free urine and a normal blood-

TABLE 9

D. Diabetes mellitus. Female, aged thirty-six.

Date.	Urine, glucose.		Blood-sugar, per cent.	Iletin.		Diet.			
	per cent.	gm.		Doses.	Total units.	Prot.	Fat.	CH.	Calories.
Nov. 28	6.0								
30	2.2	33.3	.259 ²	2	20	45	105	60	1407
Dec. 3	2.0	42.0		2	20	45	105	60	1407
8	1.7	22.5		3	35	65	140	80	1837
9	.3	2.7		3	45	65	140	80	1837
10	.3	3.9		3	45	65	140	80	1837
11	0	0	.208 ¹	2	30	65	140	80	1837
12	.4	5.9		3	30	65	140	80	1837
13	.6	11.2		3	30	65	140	80	1837
14	.7	16.9		3	35	65	140	80	1837
15	.8	10.0		3	45	65	140	80	1837
16	.4	5.0		3	45	65	140	80	1837
17	.3	2.8		3	45	65	140	80	1837
18	0	0	.199 ¹	3	45	65	140	80	1837
19	0	0		3	45	65	140	80	1837
20	0	0		3	45	65	140	80	1837
21	0	0		3	45	65	140	80	1837
22	0	0	.166 ¹	3	45	65	140	80	1837
23	0	0		3	45	65	140	80	1837
24	0	0		2	30	65	140	80	1837
25	.5	4.7	.220 ¹	2	30	65	140	80	1837
Jan. 3	0	0	.095 ²	2	40	65	140	80	1837
12	0	0	.086 ²	2	25	65	140	80	1837
19	0	0	.105 ²	2	15	65	140	80	1837
25	0	0	.143 ²	1	10	65	140	80	1837
30	0	0	.105 ²	0	0	65	140	80	1837
Feb. 14	0	0	.100 ²	0	0	65	140	80	1837

Increasing tolerance for glucose with the use of insulin; whereas it required 45 units of iletin to maintain a sugar-free urine on December 18th, a sugar-free urine and a normal blood-sugar were obtained on January 30th without insulin while the patient was on the same diet.

¹ Blood-sugar before breakfast and before iletin injection.

² Blood-sugar about two hours after breakfast.

TABLE 10

	Blood-sugar.		Glucose urine, gm. in twenty- four hours.
	Time.	Per cent.	
M. Age ten.....	5.30 P. M.	.143	21.6
A. Age eight.....	11.00 A. M.	.100	3.6
P. Age nine.....	11.00 "	.105	3.1
	11.00 "	.143	2.3

Illustrating the common occurrence of sugar in the urine of children while the blood-sugar is at a normal level; it is very difficult to distinguish these cases from true renal glycosuria. All of the above patients subsequently proved to have diabetes, 2 of them becoming very severe within six months and requiring large doses of insulin. It is obvious that in the cases given in the table it would, for the time being, be dangerous to administer insulin, in spite of the glycosuria, because of the low blood-sugar.

sugar if sufficient study and attention are paid to the situation. In the severe types this becomes practically impossible; it would require blood-sugar and urinary determinations at frequent intervals during each day and constant readjustment of diet and insulin dosage to carry on such treatment with any degree of success. Under such circumstances it is wise to allow the blood-sugar to remain constantly above normal and not to eliminate the sugar from the urine entirely. The smaller, less frequent doses of insulin are less irksome to the patient, and the physician is not shouldering more responsibility than it is humanly possible to undertake. That cases treated in this manner do exceedingly well may be gathered from Table 6; this man gained weight and to all intents and purposes attained a normal physical condition, from which he has not deviated during a period of eighteen months while his urine contained sugar and a distinct hyperglycemia existed; from the final figures on March 13th in this patient it is apparent that the provision of a "sugar cushion" serves its purpose very well, for on that date, after a very long interval, suddenly the blood-sugar values return to a low normal, although neither the diet nor medication has been changed. There is now a distinct danger of hypoglycemic shock, and consequently the dosage of insulin should be dimin-

ished or the diet raised. The actual reason for the increased response of sugar utilization after all these months is hard to determine; it may be that the particular preparation of iletin used is especially potent. However, these occurrences must be guarded against whatever their cause may be.

Hypoglycemic or Insulin Shock.—The one great danger in the administration of insulin is the lowering of the blood-sugar below the normal level. It is generally conceded that when a hypoglycemia of 0.045 per cent., or 45 mg. of blood-sugar per 100 c.c. is reached, that certain symptoms follow which may terminate fatally. These symptoms are: marked hunger, nervousness, pallor, sweating, the patient appears and acts like a person who is about to faint; a more or less violent delirium may come on, or there may be marked vertigo and weakness, to be followed by convulsions, collapse, unconsciousness, and death.

The blood-sugar level at which hypoglycemic shock appears is not constant. It varies, as do all the effects of insulin, markedly in different individuals. Thus Table 11 gives the data in a case which exhibited the hypoglycemic symptoms while the blood-sugar was at a low normal level only.

TABLE 11

Female. Diabetes mellitus.

Time.	Iletin.	Blood.		
		Sugar, per cent.	CO ₂ combining power.	
9.00 9.00 A. M.	10 un.	.183	58.6	Fasting throughout.
11.00 A. M.		.075	59.5 ¹	
1.00 P. M.		.083	53.8 ²	
3.00 P. M.		.111	52.8 ³	

Moderate hypoglycemic shock with blood-sugar of .075 per cent.

¹ 11.00 A. M., weakness, pallor, perspiration, tremor of hands.

² 1.00 P. M., same symptoms, but less marked.

³ 3.00 P. M., comfortable, but still weak.

This may be contrasted with Table 12, in which there was no ill effect even though the blood-sugar dropped to 0.052 per cent. There are cases on record in which the blood-sugar has been lower than this without producing any symptoms whatsoever, but it is not a safe chance to take.

TABLE 12

Boy. Diabetes mellitus, aged twelve.

Time.	Iletin.	Blood.		
		Sugar, per cent.	CO ₂ combining power.	
8.30 . AM.	15 un.	.326	38.5	Fasting throughout.
9.30 . AM.				
12.30 P. M.		.052	47.5	
3.00 P. M.		.064	39.5	

No signs of hypoglycemic shock, in spite of blood-sugar at level of 0.52 per cent.; seems brighter than in several days.

The treatment for hypoglycemic shock is to give the patient some readily absorbed form of carbohydrate as soon as possible, orange juice, and about 1 ounce of sugar (1 heaping tablespoonful), preferably glucose, to be repeated at fifteen-minute intervals if necessary. In unconscious or marked cases a glucose or sugar solution may be given by stomach-tube.

The rapidity with which the blood-sugar is lowered may have some bearing on the production of hypoglycemic shock. A very rapid diminution of the glycemia may result in symptoms, whereas a more conservative handling of the situation will not do so. Hence, especially in the treatment of coma patients, repeated injections of insulin are preferable to a single large one.

The use of insulin has changed the time of the appearance of the maximal amount of sugar in the urine. While dietetic treatment only was employed, it was generally appreciated that the urinary sugar increased toward evening and diminished in the morning. Table 13 shows *when insulin is injected the excretion of glucose is at its height at about 7 or 8 A. M.* In many

TABLE 13

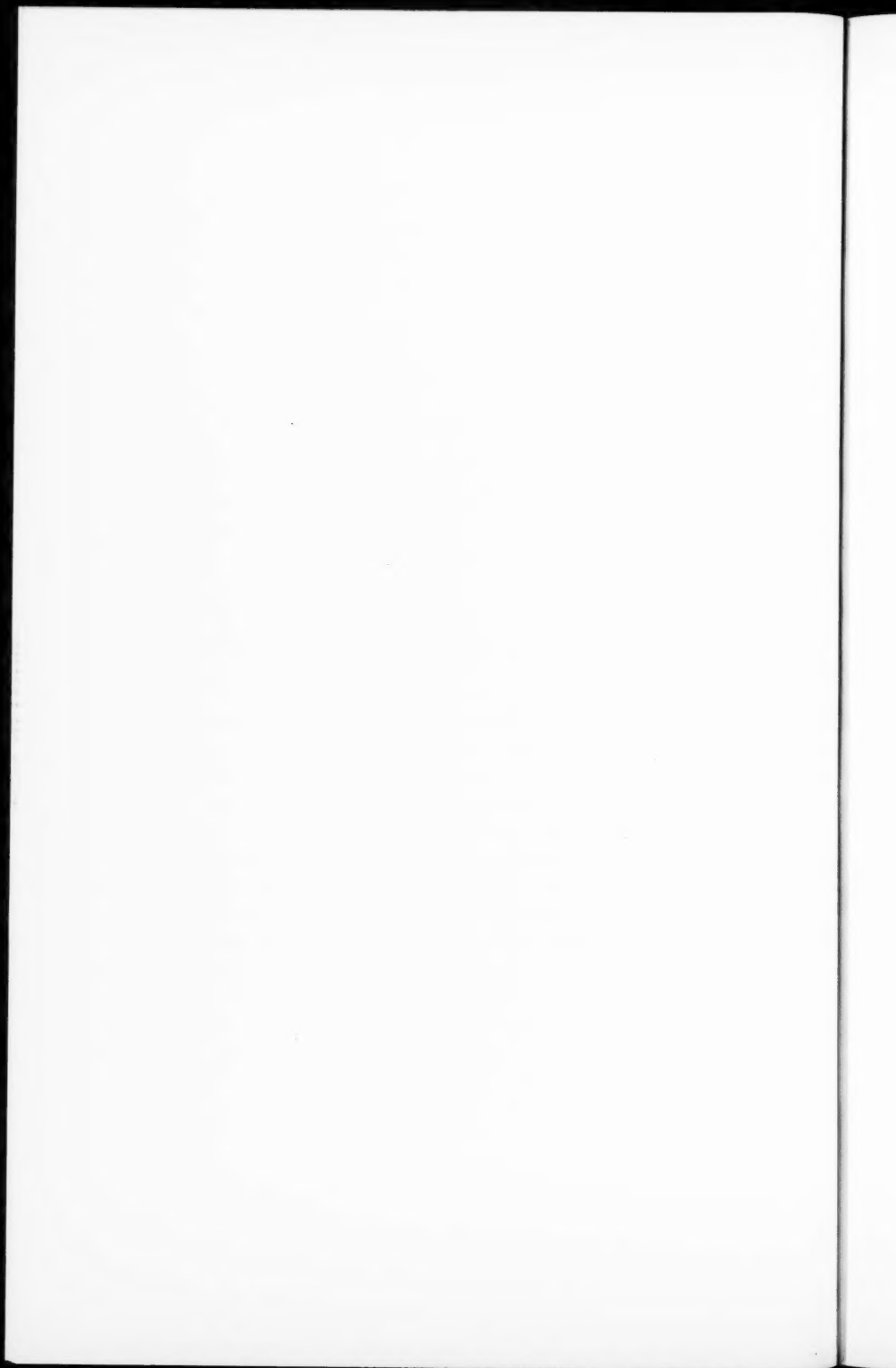
C. L. F., aged thirteen. Diabetes mellitus.

C., aged forty-four. Diabetes mellitus.

Time.	Urine glu- cose, gm.		Insulin, units.	Meals.	Time.	Urine glu- cose.		Insulin, units.	Meals.				
	Total.	Per two hours.				Per cent.	Gm.						
7.30 A. M. 8.00 "			30	breakfast	7.53 A. M. 7.15- 9.40 800. P. M.	2.5	7.6	20	breakfast				
7.30- 9.30 9.30-11.30	7.8 2.0	7.8 2.0			lunch	9.40-11.40 11.40- 1.40 1.40 P. M.	2.9 1.0			4.3 1.0			
12.45 P. M. 11.30-1.30	0.2 1.1	0.2 1.1		30		dinner	2.00 " 1.40- 3.40 3.40- 6.00 6.45 P. M.			0 0.3	1.6 0	20	lunch dinner
1.30-3.30 3.30-5.30 6.00 P. M. 6.30 "	1.5 1.5 1.6	1.5 1.5 1.6					7.30 " 6.00- 8.00 8.00-11.00 11.00- 7.15 Total			0 0 0	0 0 0		
5.30-7.30 7.30-7.30 Total	4.5 18.7	0.8							14.5				
			60						60				

Illustrates the tendency of sugar to be most marked or occur only in the morning hours; this is in direct contrast to the cases receiving no insulin, in which the evening specimen is frequently the only one that contained glucose.

instances it is extremely difficult to prevent the glycosuria at this period; the danger is that if sufficiently high doses of insulin are administered to digest the sugar during the morning hours there will be a tendency to hypoglycemic shock in the afternoon or evening. It is a rather remarkable fact that about synchronously with rising from bed the glucose tolerance is lowered; the reason for it is not at all clear. In severe cases it may be indicated to forego the temptation to control the morning glycosuria and to be satisfied if the afternoon and evening urines are kept sugar free.



CLINIC OF DR. RUSSELL L. CECIL

BELLEVUE HOSPITAL

THE COMMON COLD; ITS PREVENTION AND TREATMENT

THE common cold is a perennial problem to both the practitioner and health officer. A great deal has been written on the subject and many remedies suggested, but at the present time we seem to be nowhere near an adequate solution. If some simple and satisfactory mode of preventing colds could be worked out a great decrease could be effected in both morbidity and mortality rates for the winter months. It is safe to say that at least 75 per cent. of all pneumonias are secondary to colds. The severe forms of bronchitis and asthma usually trace their onset to an acute coryza. Many of the more unusual infections, such as meningitis, poliomyelitis, and encephalitis, date their origin from an acute respiratory infection. Furthermore, it should be remembered that not only in the infectious diseases but also in the chronic constitutional diseases the upper respiratory infections play an important part. The first symptoms of cardiac decompensation, chronic nephritis, diabetes, chronic arthritis, etc., often appear in the wake of a severe cold.

In the present clinic I shall try to get away somewhat from the conventional mode of approaching the cold problem, and attack it more from the standpoint of bacteriology and immunology. The etiology of colds is not yet settled, but a considerable amount of new knowledge has been gained in the last few years, and it is worth while to review this knowledge in relation to specific prophylaxis and treatment.

The Bacteriology of the Normal Mouth.—Before discussing the etiology of the common cold it is necessary to refer briefly to the bacteriology of the healthy mouth. The healthy nasal

cavity is sterile or contains at most a few staphylococci. The normal pharynx and nasopharynx, however, harbor many bacteria, the most important being *Streptococcus viridans*, *Streptococcus hemolyticus*, pneumococcus, usually Type IV, occasionally Type III, *Bacillus influenzae*, *Micrococcus catarrhalis*, *Micrococcus pharyngis siccus*, *Staphylococcus aureus*, and *Staphylococcus albus*. *Streptococcus viridans* and *Staphylococcus albus* usually predominate.

The Bacteriology of Acute Coryza.—In acute coryza the bacteriology of the mouth usually differs very little from that in the healthy state. In many cases, however, there is a difference in proportion, certain of the more virulent forms, such as streptococcus or pneumococcus, or *Bacillus influenzae*, becoming more predominant and remaining so until the cold is over.

However, there are many exceptions to this rule. One often sees colds caused by *Streptococcus hemolyticus*, the influenza bacillus, or the fixed types of pneumococcus, the organism in question entirely disappearing from the mouth flora within a week or two after the cold has subsided. In some experiments carried out by Cecil and Steffen acute coryza was experimentally produced in human volunteers by swabbing the nasal cavities and throat with a virulent culture of *Bacillus influenzae*. In most of these volunteers the Pfeiffer bacillus disappeared from the pharynx within two weeks after the cessation of symptoms.

The Etiology of Acute Rhinitis.—It is safe to say that all colds sooner or later are infections, but, this being granted, it is still possible to classify colds into three groups:

1. Non-contagious colds.
2. Contagious colds, and
3. Influenza, which may be endemic, epidemic, or pandemic.

1. *The Non-contagious Cold.*—The non-contagious cold may be due to any one of a number of causes. Any agent which irritates the mucous membrane of the pharyngeal or nasal mucous membrane may set up congestion, which soon becomes an acute inflammation due to bacterial invasion of the injured mucous membrane. One of the commonest causes for this form of cold

is acute indigestion. Some people develop a cold after almost any gastro-intestinal upset. I know of one patient who invariably develops a coryza after eating candy. Of such digestive disturbances there are various manifestations in the mouth, such as herpes, coated tongue, acute stomatitis, and roughening and congestion of the nasopharynx. Excessive smoking is another frequent cause of colds. Strangely enough, cigarettes appear to cause more irritation to the pharyngeal mucous membrane than cigars or a pipe. Irritating gases, such as chlorin, bromin, etc., very quickly set up an acute congestion of the mucous membrane which will usually be followed by an acute pharyngitis or rhinitis. Extremely cold air or overheated air, particularly if too dry, often predisposes to a cold. Singers and public speakers are apt to develop pharyngitis after straining the voice.

In this group must also be considered the colds, infectious but usually not contagious, which develop from local foci of infection, such as the tonsils or accessory sinuses.

In addition to the colds which are caused by some local irritation to the mucous membrane, there is another large group of non-contagious colds which depend upon some disturbance in circulation. This type of infection is seen most frequently in neurotic individuals of the vagotonic type. The instability of the vasomotor system in these patients renders them very susceptible to sudden changes in temperature. When the air is cold they are readily chilled. When they enter an overheated room they break into profuse perspiration.

Exposures to changes of temperature may cause colds in individuals with stable nervous systems, but who habitually wear either too much or too little clothing, thus exposing the body unduly to sudden changes in temperature. Grant, Mudd, and Gray have shown that when cold drafts of air are allowed to blow on the skin of healthy individuals the surface temperature of the pharyngeal mucous membrane is lowered, and following such change in temperature many of these subjects develop symptoms of acute coryza. These investigators also studied the bacteriology of the mouth before and after exposure, and found that while there was no qualitative change in the bac-

terial flora during a cold, there was a definite quantitative change, some strains becoming much more prominent in the cultures than they had been previous to the exposure.

2. *The Contagious Cold*.—The contagious cold exists in endemic form, but is also apt to appear in mild epidemics. The factors which conduce to attacks of non-contagious colds also play an important part in the etiology of the contagious cold, but undoubtedly the contagious cold is capable of attacking a healthy individual with healthy mucous membranes. Undoubtedly colds may be produced at times by almost any of the common pathogenic bacteria, but evidence is accumulating to show that many of the common colds are referable to some form of filterable virus. Foster transmitted colds to healthy volunteers by means of the nasal secretions from a case of acute coryza, and claims to have cultivated a peculiar micro-organism from the nasal secretions which he considers the exciting agent. More recently Olinsky has transmitted colds to healthy individuals by means of the nasal secretions from patients with colds, but he was not able to cultivate a virus. Both of these experimenters transmitted the infection with secretions that had first been passed through Berkefeld filters.

In the non-contagious colds infection is usually endogenous, that is, the exciting agent exists already in the nasopharynx and gains entrance to the mucous membrane through some local injury or local change in temperature. In the contagious cold infection is exogenous. It may be some virulent bacterium, usually streptococcus, pneumococcus, or some type of influenza bacillus. More frequently, however, it appears to be some filtrable virus which initiates the infection, but which is soon replaced by secondary bacterial invaders. It is important to note that the complications of coryza, either contagious or non-contagious, are caused by pathogenic bacteria rather than filtrable virus.

3. *Influenza* occurs in three forms—endemic, epidemic, and pandemic. We have very little definite information as to the etiology of this infection. We do not even know that the three different forms are caused by the same virus. Considerable de-

bate still exists as to whether the epidemic and pandemic forms are referable to the Pfeiffer bacillus or to some form of filtrable virus. The Pfeiffer bacillus can usually be demonstrated in the discharges of these patients, and there are many bacteriologists who still look upon it as the existing agent of epidemic influenza. Olitsky, however, has recently cultivated a filtrable virus from patients with influenza, and claims to have produced an influenza-like disease in rabbits by injecting them intratracheally with the virus. Olitsky's studies are extremely interesting and important, but have not yet been confirmed by other investigators.

It is not my purpose to discuss influenza in this clinic, but it is important to remember that the differential diagnosis between a severe cold and a mild attack of influenza is very difficult to make. The chief characteristics of true influenza are fever, prostration, and leukopenia, but any or all of these symptoms may occasionally be seen in a case of acute coryza.

Immunity Against Colds.—In most people an attack of coryza gives only a short-lived immunity. In general, I should say that the average cold confers an immunity of about six weeks' or two months' duration. During this time the individual can take a good many chances in the way of exposure and improper personal hygiene, and avoid reinfection. Toward the end of this period, however, any indiscretion is likely to bring on another attack. The brevity of this immunity in contrast to most infectious diseases is probably dependent on several factors. The infection is limited in extent; it is caused by organisms of comparatively low virulence, and it takes place on the surface of the mucous membrane where there is comparatively little absorption of toxic products into the system. For these reasons the amount of immunity produced is probably small and of short duration.

Prevention of Colds.—Before taking up the problem of specific prophylaxis it is necessary to emphasize certain general principles in the prevention of acute respiratory infections. In the first place, it is obvious that a person in perfect physical condition, while not entirely immune to colds, is much less

likely to have them than a person whose vitality is below normal. The first duty of the physician, therefore, is to make every effort to get the patient who is suffering from frequent colds into good physical condition. The diet must be so regulated that gastro-intestinal disturbances do not occur. The patient should live and sleep in well-ventilated rooms winter and summer. The bowels must be properly regulated. Proper clothing is also very important. I think it is unwise to lay down dogmatic rules about woolen underwear. While there are undoubtedly poorly nourished, neurotic patients who need and must have woolen underwear during the cold months, there are other patients, well nourished and "warm blooded," who are spending the greater part of their time in overheated offices, for whom woolen underwear is a decided disadvantage. The physician's advice on this subject should be determined by common sense.

A careful examination should be made for infected sinuses and chronic disease of the tonsils. Such foci should be removed if possible before any effort is made to establish an immunity with vaccines.

The treatment of the circulatory and nervous systems is perhaps the most important phase of the problem, for with good circulation and a well-regulated nervous system colds are much less likely to occur. There are three useful measures at our command—massage, baths, and exercise. Massage is valuable but expensive, and comparatively few patients will be willing to employ it. Hot and cold baths are very useful, and I much prefer the shower for this form of treatment. A few calisthenics, then a hot shower followed by a cold shower, give a tone to the vasomotor system which is not equalled by any other procedures that I know of.

The third measure is exercise, and should preferably be taken out of doors. Calisthenics, however, are valuable, and should not be despised during the cold winter months when outdoor exercise is not always practical.

Prophylactic Vaccination Against Colds.—Having improved the patient's physical condition, and having removed any pos-

sible foci of infection, the physician is now justified in turning his attention to the problem of increasing the patient's resistance to bacterial infection by means of artificial immunization. This is best accomplished by means of autogenous vaccines. I am convinced that the stock vaccine rarely if ever produces an adequate immunity against colds. There are two reasons for this—one is that the bacteria contained in the stock vaccine are usually biologically unrelated to those causing the patient's infection; in the second place stock vaccines are in most cases not sufficiently concentrated. Many of the stock vaccines now on the market are almost translucent when held up to the light. In administering stock vaccine for the prevention of colds the physician usually gives only three injections of vaccine. If a cold itself will not produce enough immunity to protect through the entire winter, how can three injections of vaccine be expected to produce such an immunity? The writer's method of immunizing patients against colds is as follows:

The patient is usually seen at the office during an acute attack, but whether he is seen during an acute attack or between attacks, the method of procedure is the same.

Cultures are made from the throat and from both nasal cavities by means of slender wire swabs. The swabs are washed off in a few drops of blood-broth and the blood-broth is then spread over blood-agar plates. Autogenous vaccines are prepared from the more important species of bacteria isolated. *Streptococcus*, *pneumococcus*, *Bacillus influenzae*, and *Staphylococcus aureus* when present are always included. The other bacteria are usually ignored. The completed vaccine usually contains two to four different species mixed in equal parts and made up to a total concentration of 2,000,000,000 bacteria to the cubic centimeter. The bacteria are killed by heating to 60° C. for one hour, and 0.25 per cent. trikresol is added as a preservative. Inoculations are started at once, the first dose being 0.1 c.c. The patient receives subsequent inoculations once a week, and the dosage is increased 0.1 c.c. with each inoculation until a dose of 1 c.c. is reached. Thereafter 1 c.c. of vaccine is administered once a week indefinitely. If at any stage of the treatment the patient

complains of general malaise or headache following the injection, the size of the dose is slightly decreased, and any subsequent increase in dosage is made more cautiously. As spring approaches the inoculations are given at longer intervals—from ten days to two weeks. I usually advise patients to continue inoculations until April or May. It is doubtful whether the immunity acquired during one season would be effective through the following winter. For this reason the writer recommends administration of vaccine inoculations for two consecutive years. By this time the patient may have outgrown the *habit* of contracting frequent colds. His mucous membrane is in a healthier state, and if he has heeded medical advice, his general physical condition is much improved.

I have employed this method of vaccinating against colds for a number of years, and during that time have treated a considerable number of cases by this method. The results have been very encouraging. Success has not been obtained in 100 per cent. of cases, but, on the other hand, there have been only a few cases of complete failure. In the majority of instances there have been no colds, or, if colds have occurred, they have been much less frequent and of a distinctly milder character.

It must be admitted that the procedure described above is not a simple method of preventing respiratory infections. It necessitates a good many visits to the doctor's office, more than most patients are willing to make in order to prevent such a comparatively mild infection. On the other hand, there are a considerable number of individuals, particularly children and young people, who have frequent colds in spite of all that can be done to prevent them by hygienic measures. Many of these patients are prostrated with each attack, so much so that they are confined to bed or at least to their homes for several days. Such individuals will gladly co-operate in any reasonable scheme which will prevent their infections.

In vaccinating against colds it is dangerous to give any sort of guarantee of absolute prevention, for occasionally one fails completely to stop the attacks. In my own experience success has been most marked in children and young people.

Treatment of Colds.—It is amazing to read in medical literature of the almost innumerable remedies that have been brought forward for the treatment of colds—everything, indeed, from a hot foot-bath to standing on the head!

In spite of these much vaunted remedies most people, including physicians, accept acute coryza with a certain resignation, and within certain limits allow nature to take her course. Passing over without comment the great majority of these cures, there are certain fundamental principles in the treatment of colds which are accepted by all. First, rest, preferably in bed; second, simple diet; third, catharsis; fourth, the use of mild analgesics, such as aspirin or pyramidon, to relieve headache and pain in the nose and throat. The old-fashioned treatment consisting of hot bath, hot lemonade and whisky, and a full dose of Dover's powder, still has many advocates.

I have been much interested in efforts that have been made to abort colds by various local or general agents. In respect to local agents I consider a 25 per cent. aqueous solution of argyrol the most efficient. It should be used in the throat as a gargle. A few drops may also be placed in each nostril with a medicine-dropper. I know of no medicinal cure for colds. Quinin still has its followers, but I cannot vouch for its efficacy. Vaccines, as indicated above, are useful only in the prevention of colds. They have no value in the treatment of a particular attack.

The Chlorin Gas Treatment.—Vedder and Sawyer have recently published an important study on the use of chlorin as a therapeutic agent in respiratory diseases. During the war they had observed that no cases of influenza occurred among the operatives in the chlorin plant at the Edgewood Arsenal, although every other organization in the arsenal had its full quota of cases. These investigators first determined the concentration of chlorin in the air necessary to kill the commoner pathogenic bacteria. They found that 0.021 mg. of chlorin per liter of air would kill most bacteria in one to two hours, and that this degree of concentration was non-irritating to the nose and throat.

In another experiment they showed that when patients in-

haled for one hour an atmosphere containing 0.02 mg. of chlorin per liter, subsequent cultures from the nasopharynx were sterile or almost so. Finally a large number of therapeutic tests were made on patients with acute and chronic rhinitis, acute bronchitis, influenza, and whooping-cough. The results were highly gratifying. In a large series of acute coryzas 74 per cent. were cured, and 23.5 per cent. improved. Similar or even better results were obtained in acute laryngitis, acute bronchitis, influenza, and whooping-cough.

The work of Vedder and Sawyer introduces a new and interesting field of therapeutics. If their experience is corroborated by other workers, the chlorin treatment of coryza and other respiratory infections will have to be ranked with the great medical contributions of this decade.

CLINIC OF DR. GEORGE G. ORNSTEIN

DEPARTMENT OF TUBERCULOSIS, VANDERBILT CLINIC,
COLUMBIA UNIVERSITY

SYPHILIS SIMULATING TUBERCULOSIS

CASES simulating pulmonary tuberculosis are often encountered in the clinics for the treatment of the tuberculous patient. In our clinic we have occasionally had patients presenting a number of symptoms which are considered almost pathognomonic of tuberculous infection of the lung, and which were, therefore, referred to the tuberculous clinic. Cough, expectoration, hemoptysis, temperature, rapid pulse-rate, malaise, fatigue, night-sweats, and loss of weight were complained of by these patients. With the above symptoms, in spite of a negative physical examination of the lungs and a normal roentgenogram, a diagnosis of pulmonary tuberculosis was made. It was believed that this type of case represented the early form of the disease in which the amount of tuberculous infiltration was too small either to produce physical findings or to cast shadows in the x-ray film.

Among this group of patients one gave a history of venereal infection. The Wassermann reaction was reported 4+. It was decided to place this patient on antiluetic therapy. The treatment rid the patient of all his symptoms. From then on a routine examination of the blood for syphilis was made on patients presenting the above symptom complex with scanty physical findings and a normal roentgenogram of the lungs. The frequency of the occurrence of a 4+ Wassermann reaction in this type of case will be best demonstrated in the following case reports:

Case I.—M. H., a male, white, thirty-two years of age, a tailor by occupation, was referred to the tuberculous clinic on August 7, 1922. He com-

plained of a persistent cough with scanty expectoration. The cough had been present for a long period. It was not annoying, but worried the patient because of its persistence. Seven months ago the patient coughed up an ounce of blood and had a blood-streaked sputum for a week following. His temperature and pulse-rate were normal. Previous history discloses a gonorrheal infection fifteen years ago.

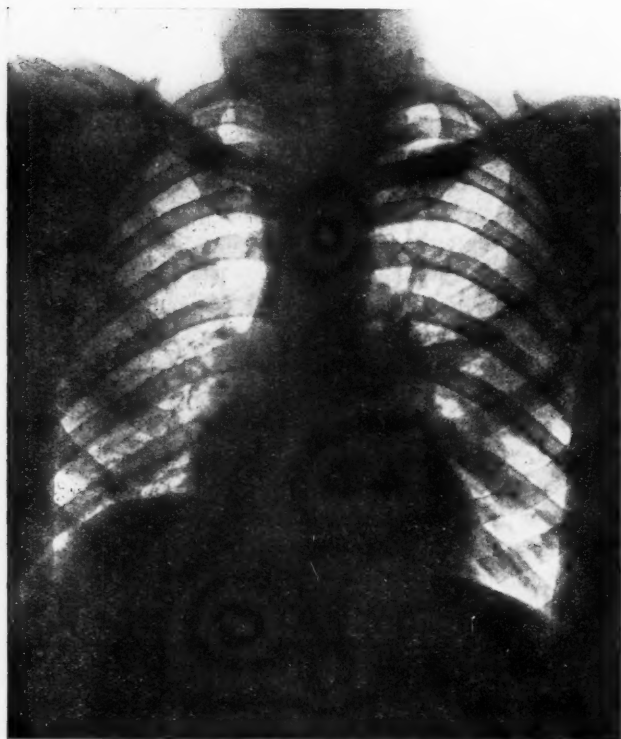


Fig. 25.—x-Ray of Case I—M. H.

Physical Examination.—Right lung: On percussion, impairment of resonance was elicited from the apex to the second rib anteriorly and the fourth vertebral spine posteriorly. Breath sounds over the above area were diminished in intensity. Posteriorly, below the eighth vertebral spine to the base, a few moist mucous rales were heard.

Left lung: No modification of the normal breath sounds were heard. x-Ray examination disclosed a normal lung picture. Sputum examinations

were reported negative for tubercle bacilli. The Wassermann reaction was reported 4+. The patient was referred to the Department of Dermatology for antiluetic treatment. Under this therapy his cough and expectoration disappeared.

Case II.—F51,313, a white female, twenty-six years of age and married, was referred to the clinic with a diagnosis of pulmonary tuberculosis.

History.—In February, 1923 she had an attack of dry pleurisy involving her right lower chest. During the latter part of April, 1923 she began to cough and expectorate. About this same period she had a hemoptysis, raising about a teaspoonful of bright red blood. She complained of night-sweats, severe headaches, and the loss of about 8 pounds in weight since the beginning of her illness. The patient was admitted to the tuberculosis clinic on May 8, 1923. At 2 p. m. her temperature was 98.6° F., pulse 80, and respirations 24. Her weight was 152 pounds. She still complained of the above symptoms. Her cough had increased in severity. Changes in posture aggravated her cough. The climbing of stairs or walking up hill easily tired her. She had no inclination to do anything. Her past history was irrelevant. There was no history of contact with tuberculosis.

Physical Examination.—There was a muscular spasm over the right upper half of the thorax. Right lung: On percussion, dullness was elicited from the apex to the third rib anteriorly and to the fifth vertebral spine posteriorly. Diminished bronchovesicular breathing was heard over the same area. No adventitious sounds were heard. Left lung: Normal breath sounds were heard.

In spite of the scanty physical findings a diagnosis of minimal tuberculosis was made. The patient was asked to return on May 10th. Her physical findings were the same as above. Her sputum report was negative for tubercle bacilli. Her temperature was 98.6° F., pulse 84, and weight 153 pounds. It was decided that with such scant physical findings an x-ray examination would bear out the almost pathognomonic history of pulmonary tuberculosis. The x-Ray Department reported a normal pair of lungs. The patient returned on May 31st. Her cough and expectoration had increased. Her temperature was 99° F., pulse 100, and weight 150 pounds. An intracutaneous injection of old tuberculin was made. She reacted vigorously to 0.1 c.c. of 1:100,000 dilution. It was determined then that this was a case indicating a very minimal form of pulmonary tuberculosis which had not enough infiltration to produce physical findings or cast x-ray shadows.

The patient did poorly on routine rest and increased diet. Her cough was difficult to control. Her temperature remained at about 99° F., and her weight decreased slowly, reaching 146 pounds on June 2d. The patient was doing so poorly that it was decided to put her on tuberculin therapy. The patient improved at first, but after the first month progressively became worse. She began to have frequent hemoptysis. The amount of blood was less than $\frac{1}{2}$ teaspoonful. On July 27th she coughed up a large clot of blood. A Wassermann reaction was done at this time, and was reported 4+. She was referred to the Department of Dermatology for antiluetic therapy on August 3d. Her temperature then was 99° F., pulse 96, and her weight 141 pounds.

Her cough and expectoration had increased. After the first injection of neo-salvarsan her cough and expectoration almost completely disappeared. On December 28th she returned to the clinic. Her cough had completely disappeared. She felt normal again and could do her days' work without becoming fatigued. Her temperature was 98° F., pulse 80, and her weight 138½

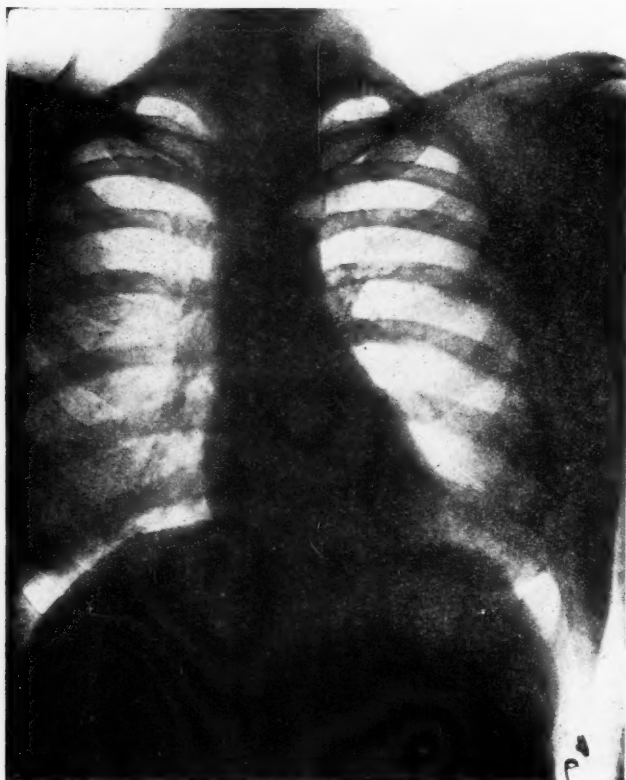


Fig. 26.—x-Ray of Case II—F51,313.

pounds. Were it not for her weight she would today consider herself normal. Her physical findings have not changed.

Case III.—No. F49,014, a school girl of fourteen; was referred from the Throat Department to this clinic on April 18, 1923. The Throat Department suspected a tuberculous larynx. One month ago the patient had become

hoarse. She began to cough and expectorate. She coughed most at night. She was not sure whether she had raised any blood, but did notice a blood-streaked sputum once. In the last six months she has lost 12 pounds. She complained of a poor appetite, which she thought might have been due to pain in her throat in swallowing. Her temperature was 100° F., pulse 146, and weight 77½ pounds. Her past history was irrelevant.

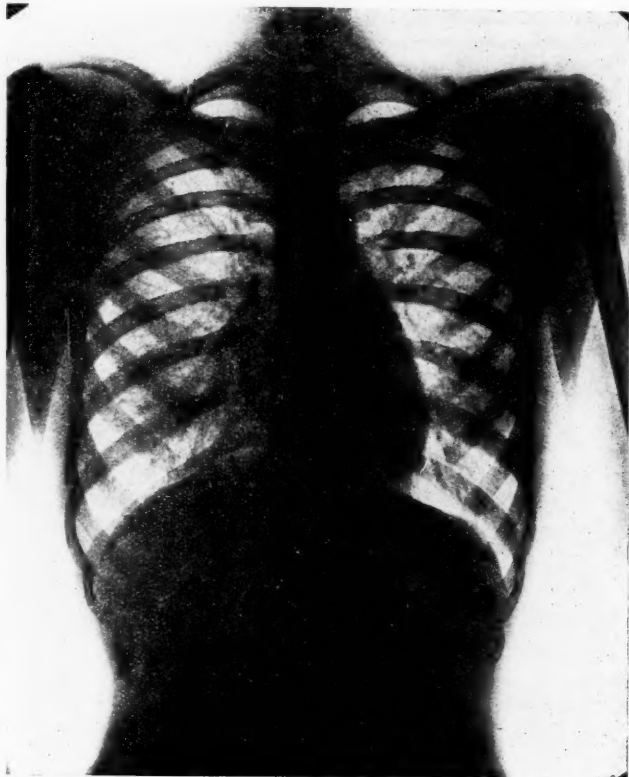


Fig. 27.—x-Ray of Case III—F49,014.

Physical Examination.—Sibilant and sonorous râles were heard over both lungs. The râles masked the breath sounds. An x-ray of the lungs was taken. The x-ray except for an accentuation of the descending bronchial trunks was negative. The patient returned the following day with a temperature of 100.8° F., pulse 152, and weight 76½ pounds. The patient was dyspneic. The findings were the same as above.

Tuberculosis was eliminated by the x-ray examination. Syphilis was suspected. Due to the precarious condition of the patient she was sent to Bellevue Hospital. There she was given antiluetic treatment at once, with an immediate clearing up of her symptoms. Blood taken for a Wassermann reaction before she was sent to Bellevue Hospital was subsequently reported 4+. This was corroborated at Bellevue Hospital. The patient returned to the clinic on September 7th. Her cough and expectoration have disappeared. Her temperature was 98° F., pulse 118, and weight 93 pounds. On physical examination her lungs were normal. She was still slightly hoarse. She was still having antiluetic treatment at Bellevue Hospital.

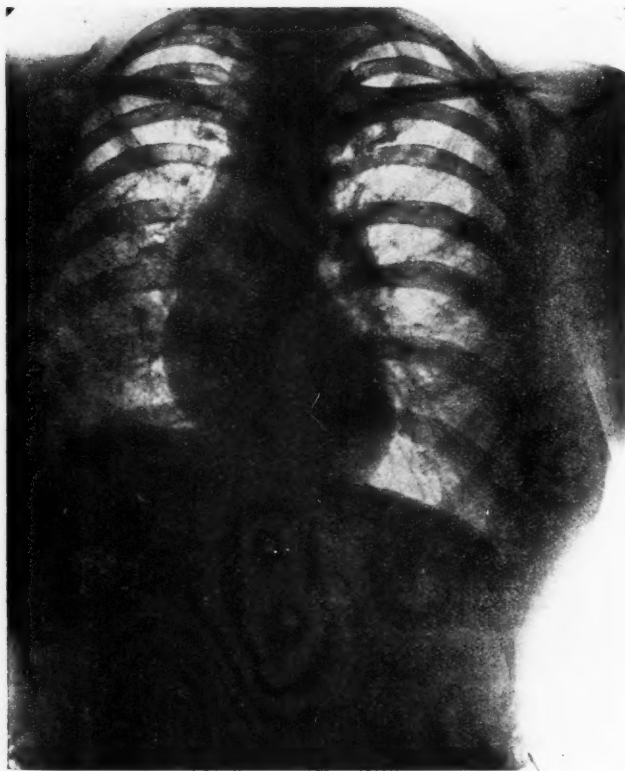


Fig. 28.—x-Ray of Case IV—F66,383.

Case IV.—No. F66,383, a white woman of forty-two years, married and an actress by occupation, came to the clinic on November 2, 1923.

History.—In February, 1923 she coughed up a mouthful of blood. Following the coughing up of blood she began to cough and expectorate. For a week following the hemoptysis her expectoration was streaked with blood, she lost weight, had afternoon temperature, and tired easily.

A diagnosis of pulmonary tuberculosis was made by her physician. The patient was sent up into the mountains, where she remained until two weeks ago. She did very well in the mountains, where her cough and expectoration cleared up. Her weight had also increased. Since her return to the city she has lost weight and her cough and expectoration have returned. One week before she coughed up a mouthful of blood. Her expectoration had been streaked for the past week. She complained of hoarseness, poor appetite, weakness, and constipation. She complained of pain in the left side of the thorax close to the sternum. Her temperature is 97.6° F., pulse 80, and weight 132½ pounds.

She has a son twenty years old who, she says, is being treated for tuberculosis of the spinal column.

Physical Examination.—A few moist râles were heard posteriorly over the right lower lobe. The heart was drawn over toward the right side.

With scanty physical findings and an x-ray examination that ruled out pulmonary tuberculosis syphilis was suspected. The sputum examination was reported negative for tubercle bacilli. A Wassermann reaction was done and reported 4+. On fluoroscopy, pulsating areas were seen over the ascending and transverse portion of the aortic arch, which were diagnosed as probable aortitis. Under antiluetic therapy the patient's cough and expectoration cleared up. The small doses of neosalvarsan had to be discontinued because of the sensation of pain which occurred beneath the sternum after each injection. The bismuth treatment was substituted and the patient improved a great deal.

Case V.—F69,252, colored male, thirty-three years of age, was referred to the Tuberculosis Clinic as an incipient case of pulmonary tuberculosis. The patient began to cough six months ago. His cough was worse during the day. There was no expectoration. The cough was very annoying to the patient. The patient tired easily with little exertion. He had lost 5 pounds in the last year. He denied having any venereal diseases. He was referred to the Tuberculosis Clinic because of his persistent and annoying cough, a slight increase of temperature in the afternoon, and the frequent manifestation of fatigue with the least exertion.

Physical Examination.—The breath sounds were normal except for being diminished in intensity posteriorly over the upper lobes. No adventitious sounds were heard. The heart was normal in size. Over the aortic area a diastolic shock was felt on palpation. The aortic second sound had a hollow-like quality. A diagnosis of aortitis was made. The Wassermann reaction was reported 4+. The patient was placed on antiluetic therapy.

His symptoms, except the cough, cleared up. He coughs a great deal less than before his treatment. He is now able to do his day's work without tiring.

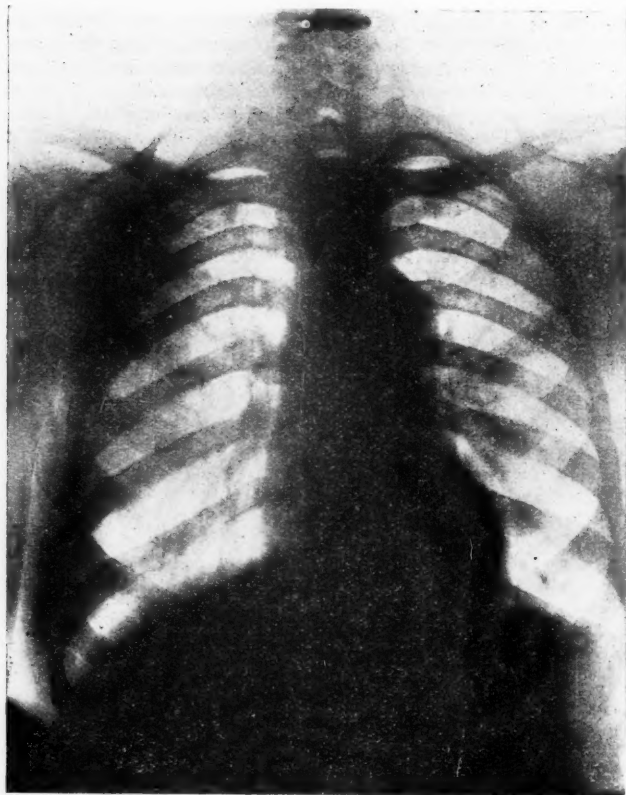


Fig. 29.—x-Ray of Case V—F69,252.

Case VI.—F70,701, a white male, forty-two years of age, came to the Department of Dermatology for treatment for syphilis. He had been informed by the Board of Health Laboratories that his Wassermann reaction was 4+. He was referred from the Skin Department because of the following history:

The patient has been coughing and expectorating for the past six years. He coughed in the morning on arising and at night upon retiring to bed. Last summer he had a persistent blood-streaked sputum. He had pain in his left shoulder. He had lost some weight, but was hazy as to the exact amount. He had frequent attacks of hoarseness. He has been very constipated. On admission to the clinic his temperature was 99.8° F., pulse 80, respirations 24, and weight 136 pounds.

Physical Examination.—Right lung: The breath sounds were decreased in intensity over the lower lobe. Moist low-pitched râles were heard over the lower lobe.

Left lung: The breath sounds were decreased in intensity over the lower lobe. Low-pitched râles were heard in the same area.

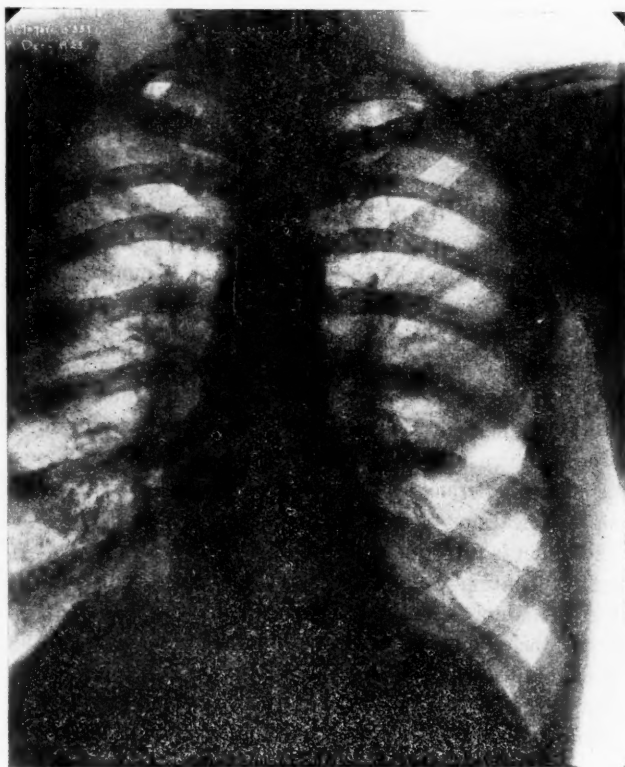


Fig. 30.—x-Ray of Case VI—F70,701.

x-Ray Examination.—Right lung: The root shadows are greatly exaggerated and extend out into the parenchyma of the lung. The root shadows are composed chiefly of fibrous tissue. There is a marked fibrotic infiltration of the descending bronchial trunks.

Left lung: The same condition exists as described above except to a lesser degree.

Repeated sputum examinations were reported negative for tubercle

bacilli. The Wassermann reaction done in the Skin Department was reported 4+.

The patient was put on antiluetic treatment. His general condition improved. His temperature became normal. His weight increased to 143 pounds. The patient felt better except that at times he had attacks of dyspnea which resembled asthmatic attacks. A diagnosis of chronic bronchitis with syphilis as the etiologic factor was made in this case.

Discussion.—The above cases are very interesting. Any one of them may be justly diagnosed as probable pulmonary tuberculosis. With a history of hemoptysis or blood-streaked sputum, cough, expectoration, and afternoon temperature pulmonary tuberculosis is to be thought of until the condition can be explained on another pathologic basis. Bronchiectasis, malignant tumor of the lung, mitral stenosis, and pneumoconiosis may also be responsible for cough, expectoration, and hemoptysis. However, the physical examination and the roentgenogram will easily bring to light the latter pathologic conditions.

When the physical findings are scanty or normal and the x-ray examination demonstrates no pathology, then cough, expectoration, hemoptysis, etc., are difficult to account for. It has been the custom to class such cases as minimal pulmonary tuberculosis. Perhaps the lesion is too little in amount to produce modifications of the normal breath sounds. The density of the lesion is not sufficient to cast a shadow in the x-ray film. Negative sputum examinations for tubercle bacilli are of no value. It is only a positive sputum that has any weight. The patient labeled minimal pulmonary tuberculosis is sent away to the mountains, where in time, as a rule, the cough and expectoration clear up.

Unfortunately, routine examination of the blood for syphilis is not in vogue in out-patient departments. If it were, perhaps a large number of so-called cases of "minimal tuberculosis" would be correctly diagnosed as syphilis. It is not proper to classify this type of case as syphilis of the lung. They are perhaps better classified as cases of syphilis with pulmonary manifestations. Probably all the cases presented above are in the tertiary stage. It is interesting to note that in none of the cases was there a definite history of luetic infection.

May we not have in the above cases a syphilitic ulceration in the larger divisions of the bronchi? May not such an ulceration account for all the symptoms of cough with expectoration, hemoptysis, etc? Would not such an ulceration in the larger divisions of the bronchi account for the negative physical findings and the normal x-ray examination? The rapid disappearance of symptoms following treatment further supports such a belief. We are all familiar with the rapid healing of syphilitic ulceration after intravenous injections of salvarsan.

In conclusion it may be stated that hemoptysis, cough, expectoration, etc., are to be considered as caused by pulmonary tuberculosis until proved otherwise. The above symptoms with negative x-ray and physical findings should suggest a possibility of syphilis. A positive Wassermann reaction or other stigmata of syphilis will corroborate such a diagnosis.

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PYELITIS

At the outset it may be well to define more clearly what is meant by the term *pyelitis*. Broadly speaking, any inflammatory process, be it acute or chronic, involving the pelvis of the kidney could be properly designated as *pyelitis*. And so, there might be a pyelitis secondary to renal infection, a tuberculous or syphilitic pyelitis, a cystic pyelitis, or that complicating stone or new growth. In common medical parlance, however, the appellation is more usually employed to signify a special variety of renal pelvic complication attended with acute or chronic symptoms and pyuria.

It is well known that the common malady, *pyelitis*, which so interests the practitioner, is usually a primary affection and most frequently attributable to the *Bacillus coli*. To comprehend the clinical pictures properly, however, and for correct therapeutic approach, something should be known of those *other* forms of complicating pyelitis or pyelonephritis that may simulate the so-called primary type.

How, then, shall we most concisely and satisfactorily unfold so intricate a theme? Let us take up the following questions: the modern conception of the mode of infection and the initial lesion; how these may progress in keeping with the nature of the offending organism and the corporal response; what the consequences are of a continuance of the infection; how these manifest themselves clinically; how cases should be managed when first attacked; the treatment of the effects of the persisting or recurring affection, and, finally, let us summarize what has been most encouraging and fruitful in a technical and surgical way in combating this malady.

General Considerations.—It would be futile when attempting to clarify the subject of pyelitis to limit the discussion to those lesions that are ordinarily believed to fall into the clinical groups, for what interests the medical man is primarily the diagnosis and then the treatment of the case, and not so much the more scientific segregation and classification of the diseases into types. And since neither the anatomic lesion, the localization of the affection, nor the etiologic factors and bacteria permits of categoric classification clinically, it would be well to approach the subject in a broad way. For practical purposes, therefore, one should attempt to elucidate the problem of infection of the kidney, restricting this only by the exclusion of specific inflammations such as syphilis and tuberculosis.

If this be our plan, we shall be able to make clear that several organisms and several anatomic lesions can bring forth similar clinical pictures, and since it may be impossible to foretell at the outset whether a given patient suffers merely from a so-called pyelitis or abscess of the kidney, a broad view is essential to the understanding of even the more constricted concepts. Having acquired a lucid interpretation of renal infection in general, it may not be difficult to comprehend the subject of pyelitis or pyelonephritis.

As the result of a multitude of new facts that have been gained by clinical and research investigations, we have now an altogether different conception of the term "pyelitis" in a clinical sense. Pyelitis in its strictly pathologic definition would indicate merely an inflammation of the pelvis of the kidney. The medical observer, however, in accordance with tradition has restricted this term to a certain clinical picture in which fever, pyuria, and pain in the renal region are the manifestations, and which were believed to be due to a primary inflammation of the pelvis of the kidney. It has been shown, however, that both anatomically and clinically it is impossible to get a categoric limitation to the term "pyelitis," for with every pyelitis there is associated at one time or another an inflammatory or other lesion of the renal parenchyma when its origin is through the blood route. Furthermore, one cannot prognosticate in ad-

vance from clinical signs alone whether a given case is one of the so-called mild pyelitis variety, or one that may result in destruction of the kidney or even terminate fatally.

It is well, therefore, to keep certain facts in mind when confronted with a case in which we have been previously wont to diagnose "pyelitis." These are: first, pyelitis is usually the result of a hematogenous infection of the kidney with secondary involvement of the pelvis; second, the changes in the kidney may be but slight and temporary, so that these are not demonstrable except in the severe cases, or, the renal lesions may be progressive and require operative intervention; third, pyelitis may be the consequence or secondary extension of infection of the renal parenchyma of various types, although the *Bacillus coli* seems to be the organism most commonly found; fourth, pyelitis may be due to an ascending infection, either lymphatogenic or urogenic (through the lymphatics or along the lumen of the ureter) and due to other predisposing causes in the ureter, neck of the bladder, or prostate; and fifth, pyelitis may be induced by irritative and predisposing moments in the kidney itself, such as tumor or calculi.

The subject of pyelitis or pyelonephritis is not a simple one. Even the classical variety seems to lose its stereotyped form when we become cognizant of the pathologic deviations that may occur. These give manifold lesions with a diverse outcome. The term "pyelitis" is, indeed, a bad name, for it does not mean an infection of the pelvis pure and simple, but signifies a complex of lesions—renal, parenchymal, and pelvic—supposedly attended with a definite course and symptomatology. Granted that the parenchymal lesions may be of prime importance, we should not extend these so as to embrace all types of inflammatory invasion, for the embolic lesions due to the pyogenic organisms in septic diseases should not be included here.

Pyelitis associated with stone may be a slow, insidious process without any of the symptoms of so-called "acute" pyelitis. Here we take it that the pelvis has become a *locus minoris resistentiæ*, and becomes the seat of inflammations attacked by the organisms that so frequently pass through the kidney.

Although it is always valuable for the medical man to become acquainted with the latest theories on modes of infection, we would sound a word of warning against the all too credulous trend of assuming that whatever is latest and is most embracing or dogmatic, is altogether true. In the case of renal infection we have seen this tendency well exemplified when one school sought to explain almost all renal infections on the theory of the ascending route, only to note most recently that the English and American observers select the blood route as obtaining in almost all cases.

For diagnostic and therapeutic purposes the mode of entry of infection should be borne in mind. To accept only the blood path would direct attention solely to those avenues that might favor invasion of the blood-stream; while to lend some credence to the applicability of the urogenic or ascending route would lead often to a correct mode of intervention. The relief of an obstacle, stricture, enlarged prostate (adenoma), or a calculus when a factor in facilitating ascending infection, might be of determining curative value.

It is because of our belief that in most, if not in all, cases of pyelitis a pyelonephritis exists, that a dissociation of these two clinicopathologic appellations is unwise. Let us define more clearly, since both terms are somewhat misleading. When you speak of pyelitis, it is not an inflammation of the pelvis associated with a nephritis in the true sense that is usually meant, but rather a simultaneous or almost synchronous affection of these two portions of the kidney through the action of the same organism. A patient suffering from an old nephritis, however, may subsequently develop a special form of pyelonephritis due to the action of one or several organisms; or, a patient with calculus pyelitis may develop a toxic nephritis of quite different causation.

In short, the term "pyelitis" as discussed here is restricted so as to designate an inflammatory lesion of the kidney and pelvis, irrespective of the hematogenous or ascending route, but resulting from the same bacterial cause.

It may not be amiss for practical purposes to point out that

it is difficult to classify renal infection satisfactorily. If we should desire to emphasize the importance of the bacteria, we would find that similar lesions and clinical manifestations may result from the activity of more than one organism. Only in so far as certain specific types of inflammation—such as tuberculosis and syphilis—produce characteristic clinicopathologic complexes, is a segregation of these warranted. It is true that



Fig. 31.—Carbuncle of kidney.

certain organisms, such as the *Staphylococcus aureus*, may produce solitary or confluent abscesses with little or no involvement of the rest of the parenchyma. To some of these types "carbuncle of the kidney" (Fig. 31) has been applied, but we must seek elsewhere for satisfactory classification when we desire clinical enlightenment.

Perhaps it would not be unwise to divide the infections of the kidney into those that are of a specific type, such as tuber-

culosis and syphilis, and those produced by the pyogenic or other pathogenic organisms. The latter produce varied lesions depending upon the following factors: the number of bacteria thrown into the kidney; the concentration or size of the bacterial conglomerate that may localize itself at any given point; the situation of the initial distribution; the virulence of the bacteria; the growth of the bacteria themselves; and the action of the bacteria on the tissues—this, in other words, the equivalent of the type of reactive response of the kidney.

It is rather enticing to subdivide the cases according to just what part of the parenchyma is involved, and as to whether abscesses are formed or not. To foretell such an eventuality in any given case, however, may be difficult or impossible, for the same organism may produce a multitude of lesions, purulent or non-purulent, under different conditions. We never know at the onset of the malady when the diagnosis appears to be pyelitis or pyelonephritis, as to the nature of the preponderating lesions, whether these are diffuse or localized, inflammatory, mildly productive or reactive, or any of those associated with the development of purulent foci. For clinical purposes, therefore, it would be well to disregard such rather appealing types of subdivision.

We will find in the further elucidation of our subject that the clinician's intent should be to prognosticate what renal damage has or may occur in a given case—non-destructive or destructive—rather from the standpoint of therapy and diagnosis than from the purely anatomic one. Let us explain:

Given a patient with acute pyelitis or pyelonephritis, we may ask: Are the changes in the kidney of a temporary nature, with little or no exudate; are they of greater intensity with an exudative inflammation; is a chronic interstitial productive inflammation produced; has the invasion been so extensive and with so many bacteria that focal areas of destruction (perhaps purulent invasion) have occurred; is the inhibitory action of the renal tissue so slight that the inflammatory process may continue and involve larger portions of the renal parenchyma; is this destructive process so great that the kidney will become

destroyed; and, finally, is the inflammatory invasion of such acuity and the toxicity so great that the systemic poisoning warrants nephrectomy?

Each and every one of these varieties may indeed result from the action of the same organism. It may readily be seen how important such an interpretation is, for in one case spontaneous cure takes place with but medical treatment; in another and more protracted type, conservative intervention may become necessary, such as cystoscopy and renal lavage to further the disappearance of the products of inflammation; in another, conservative operation may be necessary to liberate and remove the capsule of the kidney, with or without nephrotomy, thus aiding the drainage and circulatory conditions of the kidney; and, finally, in still others, nothing short of nephrectomy will suffice.

The Avenues of Infection.—It is interesting to note how the pendulum of thought concerning modes of infection has swung from one to another view, and how misleading excessive generalization as to causal avenues may be. Why need we ignore the possibilities of ascending infection, even if we do admit that in the greater number of cases the renal lesions are produced through the blood? And why lose sight of the secondary, very deleterious results of invasion from below that may be the sequence of the descending mode? That reflux into the ureter may occur has been pointed out and even emphasized by the very authors who have described the ascending path as being almost a negligible one.

Let us, therefore, be open-minded and accept both avenues as possible, or even a combination of the two. With such a viewpoint the practitioner will look carefully for both causes that may produce a blood and ascending infection. While he may try to delve into investigations of the former sources of origin himself, he will leave to the urologist the determination of whether mechanical and infectious conditions in the urinary conducting system play a rôle or not.

It is interesting to note that observations made in connection with pyelography gave an impetus to the investigation on

the possibility of ascending renal infection. The author was one of the first to demonstrate that cortical lesions could occur when collargol was injected into the renal pelvis for purposes of pyelography.¹ In 1913 it was shown (Turnbull²) that collargol may pass into the renal substance and remain there in the form of brownish streaks both in the cortex and in the medulla. The pigment is extra- and intracellular, partly black and partly brownish yellow.

The question as to whether the collargol travels to the cortex by way of the collecting tubules or by way of the lymphatics was investigated by this author in sheep kidneys and those of humans. The conclusion arrived at was that the path is by way of the collecting tubules.³

In short, evidence is at hand to confirm the old view that fluid containing silver particles, such as collargol, can ascend into the parenchyma and the inference is warranted that bacteria could also take the same path.

Concerning the Development of the Renal Infection.—In order to understand the development of renal infection it is well to be acquainted with the anatomy, in so far as the distribution of the vessels, the arteries, the veins and their relation to the glandular and secretory apparatus, is concerned. The problem resolves itself into, first, how lesions can occur in the kidney parenchyma itself, and, second, how secondary lesions are produced in the conducting system.

The production of lesions in the kidney depends upon the configuration and distribution of the vessels and their relations to the secreting or glandular apparatus. Furthermore, it depends upon certain other mechanical influences that in their turn are brought about by the relation of the kidney to the lower urinary apparatus.

The lesions in renal infection are the results of action of bacteria, of toxins, and a combination of the two. While the

¹ Buerger, *Amer. Jour. Urol.*, 1912, p. 166; *Surg., Gynec., and Obstet.*, October, 1914, p. 536.

² Kidd, *Common Infections of the Kidney*, 1920, p. 216.

³ Cf. Keyes, who argues that route is through lymphatics.

alterations must depend to a certain extent on the situation of the bacteria, they will consequently vary with the avenues of entry, but only to a certain extent. For the anatomy is such and the communications between the vascular and glandular systems so intimate, that the resulting picture rapidly vitiates any characteristic original lesions.

Clinical evidence is at hand to show that in so-called aseptic distention of the renal pelvis chills and fever may occur, with all the symptoms of acute infection. Such acute distention of the renal pelvis may be due to an obstructing calculus. The ureter catheter may relieve the retention of urine in the kidney; the cultures may be sterile, pus absent, and still the symptoms of infection may be simulated. In such instances it is not too audacious to assume that a regurgitation, as it were, of retained products through the parenchyma of the kidney with reabsorption may take place. We ourselves lean to the view that either by reflux, by reverse peristalsis, or by sudden contraction of the renal pelvis when obstruction is present, without obstructions in the lower ureter and bladder, a percolation or inhibition of fluid or foreign particles, can and does take place more frequently into the parenchyma of the kidney than is supposed.

Distribution of the Renal Lesion.—If we become too enamoured of the hematogenous theory, we might be induced to expect the renal lesions to follow the course and distribution of the avenues of supply. A careful study, however, of the extensive arborescence of the arteries of the kidney (Fig. 32) and a reference to a similar distribution of the veins, would make it evident that the vascularity is so great, the spatial interval between the capillaries and arterioles so small, that for the most part a fusion of inflammatory lesions must soon take place. It would only be in the case of embolic closure of larger vessels that infarct-like inflammatory zones were to be expected.

Then, again, the relation of the arterial system with the tubular, and then with the canalicular or collecting systems, is such that a primarily hematogenous focus rapidly becomes an intratubular one. Furthermore, the intervals between the tubules, that is, the vascular stroma, are so small that rupture into the

canalicular or tubular system may soon take place, so that a complete effacement of the primary seat of invasion results.

In short, we can expect nothing else but a rapid diffusion of infectious products in a system such as this where we have such close contact between the venous and arterial systems, and a direct association between the tubular or parenchymatous elements with the vascular tree.



Fig. 32.—Injected specimen showing venous distribution in the kidney.

The limitations in the type of infection depend not so much on the anatomy as on other factors. As examples of the latter we may mention the destructive influence of bacteria, on the one hand, the response of the tissues on the other. And so some organisms produce large quantities of local inflammatory exudate with purulent material, and degenerative changes

with necrosis; others call forth the proliferation of fixed cells, plasma cells, and a slowly reactive productive process; others only a transitory degeneration, with possibly slight intratubular exudate; still others remain circumscribed, rapidly produce necrosis and abscesses, or produce chronic abscesses of the carbuncle type; and finally, there are those bacteria that tend to

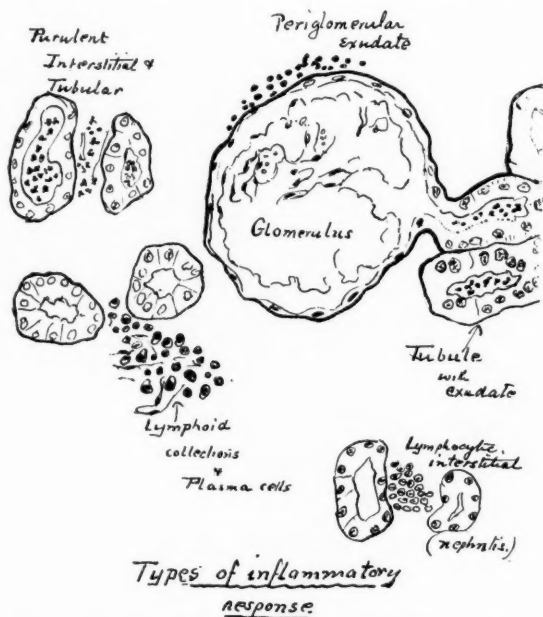


Fig. 33.—Types of inflammatory response in pyelitis and pyelonephritis: Above and to the left, combined interstitial and purulent exudate; above on the right, periglomerular exudate; below on the left, lymphoid and plasma cells in the stream; below on the right, lymphocytic interstitial inflammation.

spread over large territories, with the formation of acute exudative inflammation, with or without areas of productive proliferation (Fig. 33).

For our purposes it may be well to divide the types of renal infection that concern us here into the embolic focal infections (Fig. 34) and the less circumscribed varieties. To the embolic

type belong the typical multiple abscesses seen in the pyemic infections due to streptococcus or staphylococcus; also those larger abscesses that may fuse with adjacent ones and form carbuncle-like conglomerates, and the subcapsular abscesses that may or may not develop into perinephritic exudates. In pyelitis or pyelonephritis the less circumscribed form of inflammation usually occurs.

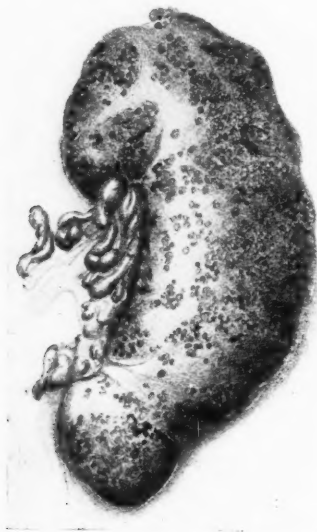


Fig. 34.—Multiple abscesses.

Multiple bacteria may enter and infect the kidney in many places but in relatively small numbers, and may invade either the circulatory elements, the tubular, or the interstitial stroma. The mild types of pyelitis or pyelonephritis may be distinguished from the severe, embolic forms in the following qualities: that the parenchymal lesions are not of a necrobiotic or destructive nature, that they are temporary, and do not form abscesses; that they form exudate, purulent or plastic without abscess formation; and that they may set up an intratubular

exudative process that is apt to subside rapidly, leaving a pyelitis or not, as the case may be.

It is conceivable, although hard to prove, that there may occur merely an exudative nephritis of the suppurative type, with little or no true inflammation of the pelvic mucous membrane. In other cases the bacteria set up a similar but less durable process in the parenchyma; the pelvis is susceptible, becomes inflamed, and its lesions outlast those of the organ itself.

As long as the lesions are of the temporary variety, limited in intensity, and as long as no permanent tubular or interstitial changes are produced, the disease belongs to the typical acute or transitory form of pyelitis or pyelonephritis.

There are other forms, varying according to the type of exudate and according to the extent and duration of the lesion. Either by reason of the heightened virulence of the organisms, their large number, or the lack of resisting power on the part of the parenchyma of the kidney, or by reason of some special tissue response, the clinical course is different. The products of the inflammation of the parenchyma are large in amount; or a hyperplastic or productive type of reactive inflammation ensues. Both of these may vary in extent so as to involve smaller or larger areas, even up to the invasion of almost all of the parenchyma. By virtue of a slowly progressive inflammation lasting for weeks, non-necrobiotic alterations may result. The colon bacillus is distinguished *par excellence* by the absence of this destructive tissue property, although a reactive tissue response—the exudate and the new cells—may vary considerably. Localized circumscribed areas of inflammatory invasion may present all transitions from small foci of the embolic type up to almost complete infiltration of the parenchyma.

For a long time the *Bacillus coli* was regarded as the most important offending agent. More recent observers have expressed the view that in pyelitis and pyelonephritis a focal infection is usually the cause, the colon bacillus being the secondary invader.¹

¹ Bumpus and Meisser, Jour. Amer. Med. Assoc., 77, November 6, 1921, p. 1475.

Indeed, Bumpus and Meisser¹ claim that bacteria obtained from possible foci in patients affected with pyelonephritis could be shown to have a selective localization for the urinary tract in experiments on laboratory animals. In 82 rabbits injected with strains of a green-producing streptococcus obtained from the teeth, tonsils, urine, and blood of patients suffering with pyelonephritis, 63 animals showed lesions in the kidneys. These findings the authors regard as evidence in favor of the conclusion that pyelonephritis may often be due to focal infection harboring streptococci; that the latter have a selective affinity for the urinary tract and that the *Bacillus coli* is commonly found and generally believed to be the cause of secondary infarction.

These authors are of the opinion that the teeth and tonsils may be the source of the infection, even if there are no apical abscesses demonstrable in the x-ray plates. Similarly in the case of the tonsils, enlargement or pus by expression need not necessarily be present to warrant assuming these as the nidus of infection.

In a series of experiments cultures were made from both teeth and tonsils, and seven series of bacteria were injected intravenously in 26 rabbits, 21 of which showed lesions in the kidney at necropsy. There were lesions in both kidneys and the bladder in 2, and lesions in the ureter in 1. Extra-urinary lesions were relatively slight compared with those of the urinary tract.

As for the kidneys, the picture of diffuse parenchymatous nephritis was absent in all instances, and there was merely localized infection. In the cortex there were often opaque yellowish-white areas, especially in the medulla, sometimes associated with areas of hemorrhage, varying in size from 1 to 4 mm. Varying numbers of necrotic areas were found in the medulla, some very small, scarcely visible, others large, grayish white streaks, gradually disappearing as they approach the cortex. Microscopically the glomeruli were found wholly free from the lesion, other than varying degrees of congestion. The necrotic areas showed marked destruction of epithelium and marked

¹ Loc. cit.

leukocytic infiltration. The parenchymatous cells around these areas were granular and swollen, and the nuclei of many cells failed to stain.

These observations appear to the author to show merely that embolic lesions of a necrotic nature are producible by the injection of bacteria into animals intravenously. Certainly the lesions produced are not at all similar to those found in the human being.

Have those researchers who would establish the dictum of the specificity of certain organisms for the kidneys accomplished much of importance? To show that streptococci taken from the teeth or the tonsils could be made to produce necrotic embolic lesions in the kidneys of animals more frequently than in other organs, must not be interpreted as proving that the same occurs in the human being. A reference to the results of animal inoculation (Bumpus¹) shows that not only were lesions produced in the kidneys of animals, but in the muscles, joints, stomach, endocardium and myocardium in first and second passages through animals, although, it is true, after the third passage only the kidneys seem to be involved.

Furthermore, to demonstrate that the colon bacillus from the urine of patients does not possess specificity for renal tissues, because lesions could not be discovered in rabbits inoculated intravenously by such organisms, does not at all prove that the organisms in question are incapable of affecting the human kidneys. The *Bacillus coli* is usually a non-virulent organism, and may require special conditions in the human to manifest its toxic properties.

At best it can be said that the experiments of some of the recent authors have shown that embolic lesions can be produced in the kidneys of animals, which is not surprising. But a reference to the type of lesion brought about in these animals will make it clear that they are necroses of the embolic type, and different from the human lesions usually seen in pyelitis and pyelonephritis.

To concede further that the *Bacillus coli* is always a second-

¹ Bumpus, Jour. Amer. Med. Assoc., 1921, 77, p. 1478.

ary invader is not altogether acceptable. It is true that certain special conditions may be necessary in the human to make possible the growth, development and toxic action of the *Bacillus coli* in the human kidney. These conditions may be brought about by the action of other organisms, it is true, but not necessarily by the growth of the organisms themselves. May not they be indirectly due to the circulating toxins of these organisms?

Then, again, we know too little as yet of the symbiotic action of two organisms. Although the less virulent one may not be able to produce focal lesions experimentally, the presence of the toxins of another or the biologic activities of another, may suffice to lend to the organism the necessary qualities of virulence.

Clinical Forms.—It would take us far beyond the scope of our presentation were we to attempt to picture to you all the many clinical forms that infection of the kidney may present. Let us confine ourselves, therefore, to but a very few exceedingly significant varieties.

You will obtain a most illuminating insight into both the symptomatology and clinical course of renal infection, if you will keep in mind the fact that by virtue of their connections with other important conducting structures lesions of these organs may almost immediately produce a train of secondary deleterious changes. These affect the pelvis of the kidney, the ureter, the bladder, the urethra and the adjacent or connecting sexual organs. You must, therefore, regard renal infection in terms of renal lesions, pure and simple, either inflammatory or toxic in nature, with concomitant damage of function; then also, in terms of the alterations that may occur in the pelvis and the obstructive influences on the narrow ureteropelvic junction; further, in regard to the mechanical changes throughout the tract and such as may result from inflammatory and obstructive influences; also in terms of the complications, such as stone, stricture, and renal parenchymal attenuation. Finally, in addition to the immediate and late morphologic changes, we must not neglect the importance of that acquired tendency to renewed infection that such kidneys may develop.

Acute Typical Pyelitis.—We need hardly dwell for any length of time upon this well known malady. It may not be amiss, however, to point out that not infrequently some evidence of the hematogenous picture of this affection is present in the form of acuteness of onset. And so we may note that there is sudden fever with chills, sometimes vomiting and headache, suggestive of some acute malady; or a history of such onset may antedate by a variable period of time the advent of localizing symptoms, pyuria, or cystitis.

It is because of the predominance of the general symptoms, fever, nausea, headache, and similar phenomena, and the absence of renal tenderness and enlargement in many of the cases, that the disease is so often unrecognized, and that a subsequent pyuria is interpreted rather in the light of a complication than as a part and parcel of the primary malady.

If we would summarize the important manifestations of an attack of so-called acute pyelitis, we would include the following: evidences of acute onset such as have been described, or an absence of these; pyuria, symptoms referable to the kidney, bladder, and urethra. Either at the beginning or after a variable period of time, there may be renal pain in one or both loins, with or without radiation along the ureter. Strange to say, this may be absent in some of the cases, so that pyuria may be the only feature suggestive of renal or vesical involvement.

Vesical symptoms, on the other hand, are almost always present, and the urgency and urinary frequency, sometimes strangury, may be the most striking manifestations of the inflammatory process within the renal organs. While these bladder symptoms are not necessarily indicative of pyelitis in the male, and may often be due to prostatitis or urethritis, they are significant of pyelitis in a large percentage of cases in the female. The urinary frequency may be striking in its intensity early in the disease and gradually abate, or may run a protracted course, depending upon the persistence of a complicating bladder or prostatic inflammation. Not infrequently hematuria may be noted, and even a urethral discharge may be set up by the supravescical infectious products.

Clinical Course.—If we try to relate the symptoms to the pathologic lesions, and bring these into harmony with each other, we can readily understand that the extent and gravity of parenchymal involvement, the intensity of the pelvic complications, as well as the susceptibility of the ureter, bladder and prostate to the given infection must all play a rôle. While the parenchymal lesions may be slight and rapidly abate, the consecutive changes in the pelvis, ureter and bladder may be much greater and more persistent. And so we can explain that often cystitis alone is complained of, and may continue for a long time. Indeed, it is this peculiarity that has so often led to the assumption that the cystitis is primary, the pyelitis secondary. It is the deviations from the typical picture that are so instructive and emphasize the importance of cytoscopic investigation of most cases of so-called cystitis, lest an infection of the kidney, uni- or bilateral, be overlooked.

The Acute Form of Pyelitis or Pyelonephritis.—Neither at the onset, nor well along, nor during the first few days of an attack of acute pyelonephritis or pyelitis will it be possible to estimate whether such an attack involves normal, previously healthy kidneys, or whether previous disease with or without symptoms had not existed. There are insidious chronic forms with uni- or bilateral involvement, possibly associated with previous symptoms of lumbago or none at all, in which acute symptoms suddenly appear due to recurrences or exacerbations in either kidney. Or there are forms in which the acute manifestations are due to retention of urine in the kidney. In others an extensive, localized, circumscribed, or diffuse pyelonephritis, suppurative or non-suppurative, complicates an old chronic affection, and still the clinical signs may be indistinguishable from those cases in which a virgin attack makes its appearance.

And finally, it may be worthy of bringing to your attention those instances in which one or more stones are present, possibly secondary to the previous infection, and one of these causes a blockage of the ureter, acute retention with a lighting up of the infectious process.

It is evident, therefore, that all of these possibilities must be kept in mind, and the discriminating clinician will not tarry too long ere he resorts to those methods of investigation—cystoscopic and radiographic—which alone can give him an adequate estimate of the anatomic and pathologic conditions present.

Subacute Pyelitis Simulating Appendicitis.—Occasionally cases confront us in whom the diagnosis of appendicitis has been made, even by the best of surgeons. Pain in the right iliac region, associated with gastric symptoms, indigestion, nausea, constipation, may be wholly due to infection of the right urinary tract with ureteritis, pyelitis and periureteritis. The distinguishing factors, however, are the presence of pus in the urine and the findings at cystoscopy.

Cases With Cystitis Symptoms.—There are cases in whom the manifestations begin with symptoms referable to the bladder, urgency, strangury, and pus in the urine, in whom the diagnosis of cystitis will be made, and in whom frank evidences of renal involvement do not make themselves manifest to the practitioner. The bladder disturbances may be wholly referable and primarily due to renal disease, which remains unrecognized. There may be no renal tenderness and even fever may be slight or evanescent, and missed by the patient or physician. Some of these cases may be seen weeks or months later, when they present themselves because of a chronic bladder affection, chronic trigonitis, or apparently incurable cystitis. Only the cystoscope will enlighten us as to the true origin of the trouble.

Acute Pyelonephritis Requiring Operation.—These cases demand some form of intervention, either decapsulation with drainage or nephrectomy. Most of the acute cases requiring operative intervention, except the fulminating cases of multiple abscesses or fulminating, acute, purulent infection, belong to a more or less chronic variety in which acute exacerbations take place. Certain exceptions to this, however, will be discussed elsewhere, where a slowly progressive form will be described that does not respond to cystoscopic and medical treatment.

The patient may have had attacks of pyelitis or pyeloneph-

ritis in the past, of which he may not be cognizant. Indeed, in many the symptoms may be those of chronic or recurrent cystitis. Throughout this time he has had a dormant pyelonephritis. Then suddenly there occurs a severe exacerbation which we call pyelitis or pyelonephritis. In some of these, chronic changes in the kidney already exist, with or without marked perinephritis, dilatation of the pelvis of the kidney, and changes in the ureter. In such, when acute infection supervenes, decapsulation and drainage may be necessary.

What better lesson can we draw from these facts than that all cases with symptoms of cystitis should be carefully investigated, lest a unilateral or bilateral chronic pyelitis remain unrecognized, a condition which is a constant menace to the patient?

Progressive Type of Pyelonephritis.—It is very difficult to determine at the outset whether a case will terminate spontaneously, whether the lesions in the kidney will disappear, those in the pelvis predominate, persist, or whether the complications will not become a feature. There are other cases, however, in which the lesions are mostly parenchymatous, and where the latter persist, continue and involve a large portion of the kidney. In these, early operation may be indicated.

Two cases will clearly illustrate: the first, a woman with bilateral pyelitis, in whom bilateral decapsulation and nephrotomy became necessary, whose kidneys showed a diffuse parenchymatous inflammatory process, involving at least two-thirds of each, but in whom the operative procedure brought about an excellent recovery.

The second case exemplifies that variety in which the exudative and plastic elements involved the whole kidney, with destructive influences, so that nephrectomy became necessary.

Case I.—*Acute, bilateral pyelonephritis; operation; recovery.* S. K., a female aged thirty-two, aborted during the eighth month (October 27, 1921). During the period at the hospital the patient complained of pain in the left lumbar region, accompanied by vomiting and temperature.

When cystoscoped by the author December 2d, with the temperature at 103° F., there were marked changes in the bladder, with an obstruction at

25 cm. in the right ureter, which was overcome. Thick pus was obtained from the right kidney, occasional pus cells from the left.

The diagnosis of bilateral pyelitis and pyelonephritis with onset on the left side was established.

From the 2d to the 21st of December numerous cystoscopies demonstrated that the infection of the left kidney was subsiding, but that the right was delivering more pus. The right kidney was tender and somewhat enlarged. During this period the temperature ranged from 99° to 104.6° F.

Operation December 24th, right nephrotomy, decapsulation, and drainage, revealed a markedly diseased kidney. On stripping the capsule extensive alterations of the surface were visible with areas of infiltration of a subacute and inflammatory nature, a grayish-yellow discoloration of the parenchyma occupying the larger portion of the external surface.

Microscopic examination showed a marked leukocytic infiltration both in the lumina of the tubules and in the interstitial tissue, with degeneration of the renal epithelium. Collections of leukocytes distributed about the glomeruli formed dense zones of cellular elements.

Diagnosis: Diffuse suppurative nephritis with more interstitial involvement than tubular.

Because of the continuation of temperature and the large amount of pus present in the left kidney specimens, this kidney was exposed January 9, 1922, and a condition similar to that in the right found; more than two-thirds of the parenchyma were yellow and diffusely infiltrated.

Histologic examination showed two lesions, one a diffuse purulent inflammation without any tendency to circumscribed agglomerates, and another subacute, more productive type. The latter presented a combination of lymphocytes, plasma cells, and polynuclear leukocytes. Even in that portion of the cortex which was macroscopically normal, the glomeruli showed exudate in Bowman's capsule, leukocytes, and immediately about them collections of polynuclear cells. Here, too, there was a diffuse suppurative process of slight extent.

The subsequent course was uneventful, the patient making a splendid recovery, and when last seen (March 26, 1923) was in the sixth month of pregnancy, with a phenolsulphonephthalein output of 28 per cent. in two hours.

Case II.—*Acute pyelonephritis, diffuse suppuration necessitating nephrectomy.* When the process is of a destructive nature, the renal tubules become broken up early. There is very little lymphocytic and plasma cell reaction, and the kidney becomes gradually destroyed. In Case I. L., female aged fifty-one, there was an indefinite history of pain on urination, pus in the urine, and temperature. Cystoscopy (April 13, 1921) revealed moderate diffuse cystitis, with pus in both kidney specimens, more clumps in the right.

Decapsulation and nephrotomy, right, April 15th, showed multiple areas of parenchymal inflammatory infiltration. This did not relieve the temperature which was up to 103° F., and on April 27th subcapsular nephrectomy was carried out. A succulent kidney covered with purulent exudate was delivered, with necrosis of the tract in which the tube had lain, the kid-

ney being edematous and degenerate. Immediately after the nephrectomy the temperature came down.

Histologic Examination.—Two types of lesions were present, first, the foci of suppuration, and second, a diffuse suppurative interstitial and parenchymatous inflammation. Despite the absence of macroscopic signs of parenchymal suppuration, the microscope evidenced extensive cellular disintegration cells, pus cells, eosinophils, and plasma cells. The stroma is largely increased in width everywhere by similar infiltrations which are also present in the tubules. *The latter are extensively destroyed, invaded by inflammatory cells and disrupted in many places*, so that they have become mere aggregations of cells without tubular arrangement. In some of the suppurative areas the tubules are represented by but a few degenerate cells. Even where the general structure of the tubules is intact, the cells have undergone marked degeneration and the tubules are filled with pus.

Clinical Classification.—To the practitioner it will be of exceeding interest to be able to group concisely the usual course of the ordinary acute cases of pyelitis or pyelonephritis. They fall into the category of those that are non-operative and those that are operative.

Of the non-operative forms there are, first, those that subside spontaneously; second, those that run a protracted course and require cystoscopic intervention and treatment; third, those that gradually, either at the first attack or after a subsequent attack, lapse into what is known as the chronic form or chronic pyelitis; and fourth, those relapsing forms in which restitution to the normal seems to take place after each attack. In this classification, however, we have not taken cognizance of those chronic cases with more or less extensive alterations of the kidney, with attenuation of the parenchyma, more or less hydronephrosis, and an obstructive condition in the lower tract which shall be referred to later.

Pathologic Classification in Relation to Treatment:

A. Minimal, evanescent or non-ascertainable lesions:

- (1) Acute inflammation, parenchymatous inflammation or degeneration, with slightly purulent exudate of evanescent type. This is followed by
 - (a) Acute pyelitis,
 - (b) Persistent pyelitis,
 - (c) Recurrent attacks.

B. *Acute type, with definite lesion, non-destructive:*

- (1) Localized purulent exudate (self-limiting).
- (2) Localized purulent and productive exudate (self-limiting).
- (3) With progressive, diffuse, purulent and productive exudate, requiring operation, but limited thereby.

C. *Destructive type (disintegrating):*

- (1) With progressive, diffuse, purulent, but destructive lesions (some reactive, productive), nephrectomy, decapsulation not being satisfactory.
- (2) Fulminating cases with multiple abscesses, with unusual toxicity (nephrectomy indicated not so much by reason of the immediate destructive influence, as because of the acute toxicity).

Let us consider what may occur if restoration to normal does not take place after an acute attack of pyelitis or pyelonephritis.

First, the kidney pelvis may be apparently restored; and still, if examination with the cystoscope could be made frequently enough, a persistence of the purulent exudate would be demonstrable;

Second, the lesions have become frankly chronic;

Third, there are relapses;

Fourth, there are frequent recurrences.

It is not sufficient for the practitioner to be satisfied that an acute attack has subsided, and to dismiss the patient with the assurance that he is cured. On the contrary, it is just as important to keep him under observation in the convalescent stage; and, even after this it is essential to watch the urine for persistence of pus; for recurrent symptoms of cystitis, for occasional lumbar aches, lumbago or abdominal cramps, or for attacks of malaise with or without slight temperature. All of these indicate that the trouble is not altogether a thing of the past.

Changes in the Kidney and Lower Urinary Tract.—As a result of an insidious infectious process or because of recurrences and as the result of mechanical effects of retention, certain chronic

changes soon make their appearance in the pelvis of the kidney, at the ureteropelvic junction, in the ureter and bladder. These may extend so as to involve even the ureteral orifice in the bladder, the bladder musculature and mucosa itself, as well as the neck of the bladder and the organs in connection with the latter.

It is well to know that in the urinary tract an inflammation of the mucous membrane does not mean that it is confined to this layer, for invasion of the deeper parts soon takes place; the underlying musculature begins to suffer, its elasticity becomes lost; the elastic fibers give way, and permanent tonus alterations take place that make for stagnation, retention and back pressure. So important is this fact that we may dwell for a moment upon it to emphasize that not only is this process of dilatation and relaxation of the collecting system (ureter) the result of chronic inflammatory processes, but, by virtue of stenoses that may take place at narrowed points, an added mechanical factor supervenes to distend the conducting system still further.

And so we may succinctly state the changes you may expect to find in the chronic cases of pyelitis and pyelonephritis as follows: the kidney pelvis becomes chronically thickened, dilated, and the parenchyma attenuated, varying degrees of hydronephrosis ensuing; the ureter suffers, its wall becomes thickened, relaxation and gradual dilatation occurring. Here and there are narrowings and the lower end of the ureter may develop a stricture. Further dilatation occurs; the ureter may become tortuous, and secondary stones may form in it. And so, losing its contractility, a cesspool for stagnant urine and pus is developed. About the kidney as well as about the ureter a chronic inflammatory process may take place, adhesions, fibrosis, and varying degrees of encasement of these structures in fatty and fibrous tissue resulting.

Allusion has been made to the tendency to stricture at the ureteral orifice. In the bad cases the bladder may become thickened, and by virtue of increased urinary frequency and spastic micturition regurgitation and reinfection from below, in the ascending sense, may take place.

So, in line with what we have said, we find two large groups

of cases of the chronic sort, both of which show the results of ureteral and renal damage. In the first the ureter is dilated, the kidney is damaged, and possibly stretched with more or less chronic retention in the ureter, sometimes with stricture either at the ureteropelvic junction or at the bladder. Many of these cases when bilateral can be treated with the cystoscope, improve, and remain tolerably well. They belong to the ambulatory cases. The lesions must be recognized, else improvement cannot take place. Suppurative infarction may eventuate at any time, and the kidney reinfected, the cortex destroyed and nephrectomy may become necessary.

The second type of case is one in which the mechanical conditions have become such that drainage is no longer adequate, even though the stricture be dilated and cystoscopic flushing of the kidney be frequently carried out. In short, nothing but nephrotomy, with or without decapsulation and temporary or permanent drainage, may be required. These cases are even more liable to suppurative infarction, and if permanent nephrotomy is not carried out early, the kidney is usually lost. When bilateral changes are present, the importance of early nephrotomy can be easily understood.

Treatment.—If we have well understood the pathologic alterations in these forms of renal infection with their intrinsic and more remote effects on the conducting system, the rationale of modern therapeutic approach will have been anticipated. Two problems always confront us—first, the immediate care of the patient; second, the prevention of destructive lesions of the kidney.

Our aim will be to concern ourselves more especially with those preventive measures that are in the practitioner's hands and may save many a kidney and often the life of a patient. How can you best accomplish this?

1. Watch for a perpetuation of an acute pyelonephritis in the form of a persistent pyelitis, ureterocystitis, with complications in the bladder or prostate.

2. Remember that such a continuance of the infection may go on without other symptoms than pyuria.

3. Interpret even vaguely suggestive symptoms—backache or lumbago—in their proper light when associated with pyuria.

4. Do not allow an acute pyelonephritis to continue, but recognize it in due time as of the progressive type, intervening then by proper operative procedure lest the kidney become destroyed.

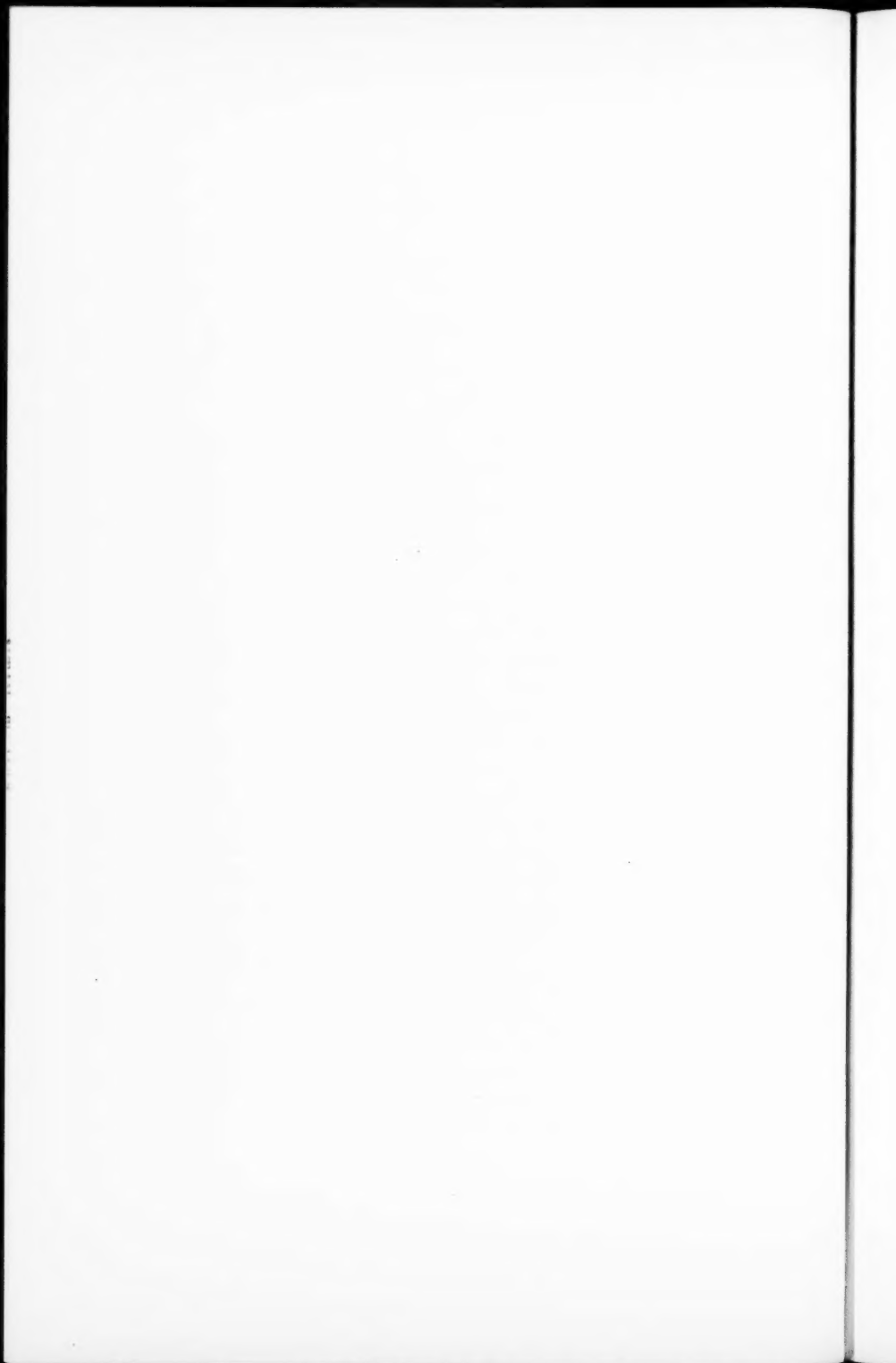
5. Do not forget that the fulminating type can be attacked only with drastic measures, namely, nephrectomy.

In the acute cases of pyelitis medical treatment will usually suffice, and the alkali treatment is advised. When the symptoms do not abate, however, after a week, it is well to remember first that urinary retention in the pelvis of the kidney may be at fault, and perhaps a complicating stone that has eluded our diagnostic methods may cause blockage. The introduction of a ureteral catheter with renal lavage may at once change the clinical course into one of immediate progressive recovery.

So, also, when the cystoscope fails you and the temperature continues, remember that it is less harmful to intervene too early than to allow the destruction of the renal parenchyma to take place, and the procedure recommended is either decapsulation alone or this with buttonhole drainage of the kidney pelvis. Many are the cases in which you will find extensive purulent infiltration of the parenchyma, and most of these you will promptly benefit in this way. In a very few, however, where the progressive type of destructive, diffuse, suppurative lesions is at hand, nothing short of nephrectomy will answer.

In the chronic cases, too, the secondary lesions in the ureter, the dilatation and the stricture, must receive frequent attention with the cystoscope. Drainage with the ureteral catheter and dilatation of the stricture will often cure or improve what you may regard as chronic and incurable pyelitis. And then it is well to get an occasional appraisal of the permanent drainage that has occurred in the kidney of the chronic cases. When distention of the renal pelvis leads to poor drainage, when with such, recurrent acute attacks take place in spite of cystoscopic care, you will have to consider the advisability of either a temporary or permanent nephrotomy. Which of these procedures

is best in the given case is a matter of delicate balancing of the mechanical and infectious factors that are at work. Certain it is that many kidneys are lost because of the prejudice against wearing a tube permanently. When you will have conceded, however, that an infected kidney, in which you are unable either by cystoscopic or temporary nephrotomy to re-establish adequate drainage, will ultimately become destroyed, then only will you choose the lesser of these two evils—permanent drainage. But you will prolong thereby the life of the kidney and also of the patient.



CLINIC OF DR. N. E. BRILL

MOUNT SINAI HOSPITAL

CHRONIC HEMOLYTIC ICTERUS COMPLICATED BY A MYELOID LEUKEMIA

THE patient whom I now present is one who not only has an uncommon disease, but a complicating factor which by the most of you would be considered as the disease itself, and the disease which I believe exists you might consider to be the complication, or, there may be present two concurrently existing diseases.

First of all, a glance at the patient reveals two definite abnormalities of more than uncommon interest, the one a marked abnormality in color, the other an evident retardation in development. The color of the patient may be described as a pale brownish green. There is no doubt of the pallor element, which is substantiated by the pale appearance of the conjunctivæ, the lips, and the gums. While the green color is distinctive, such a shade of green has most likely never been seen by any of you in a patient; it has been seen by me only once in one who was in the agonal stage of death from pernicious anemia, in whose blood were evidences of a tremendous activation of the hemopoietic system as demonstrated by the presence of primordial erythroblasts, of all types of embryonic myeloid elements and of histiocytes in the blood which were phagocytosing the red blood-cells. The green element in the color is also suggestive of the disease chlorosis, which is fast disappearing in this country, though when I was a medical student it was common, particularly among young girl domestic servants. In this patient the color approaches the shade of green sometimes seen in the metaplasias characterizing the so-called tumor designated chloroma, which occasionally is an accompaniment of lymphoid and myeloid leukemia.

The other factor, the retarded development, is shown by the small stature, the childish features, the absence of pubic hair. I am sure that if you were asked as to the age of this patient you would answer eleven or twelve; she is, however, in her nineteenth year. We shall revert to the infantile type later when we discuss the differential diagnosis.

Inasmuch as certain elements in her history may lead us to a tentative judgment which may be confirmed on physical examination I shall ask the house physician to present her anamnesis.

History.—Sadie ———, aged eighteen years, U. S.

Chief Complaint.—Weakness and shortness of breath of five months' duration.

Family History.—Father died of cancer, otherwise negative. No other member of family with jaundice or similar disease.

Past History.—Healthy at birth, no jaundice. Whooping-cough, measles, scarlet fever; grippe at seventeen. *Has always been pale as long as she can remember.*

Present Illness.—Five months before admission patient began to feel weak, so much so that she had to cease work and went to Fordham Hospital. She grew worse there, having frequent nosebleeds on the slightest trauma, becoming dyspneic, and noticed swelling of the feet and abdomen for the two weeks previous to admission to this hospital. For two months she has noticed lumps in her neck and axillæ. She has lost 15 pounds in this time. More recently color of eyes was noticeably yellow, and that of the skin of her body greenish.

Summary.—*Past History.*—Scarlet fever, measles, pertussis, grippe.

Present Illness.—Five months' duration; weakness and shortness of breath; bleeding from nose on slight trauma; edema of feet; swelling of abdomen; lumps in axillæ and neck; loss of weight; fever; abnormal color.

Physical Examination.—Poorly developed, emaciated pale young girl, resting in bed, not acutely ill, not complaining, markedly jaundiced; color of conjunctivæ and of skin of entire body an unusual very pale light green.

Eyes.—Pupils react to light and accommodation. Other reactions normal.

Ears normal.

Nose.—Externally negative. No perforation.

Throat.—Teeth in poor condition, cavities; tonsils enlarged and diseased.

Neck.—No rigidity. No petechiæ. Thyroid just palpable. Numerous large lymph-nodes along the anterior and posterior cervical chains, also enlarged submental nodes.

Chest.—No abnormalities. Skin shows large number of purpuric spots.

Lungs.—Entirely normal.

Heart.—Apex in fifth space, in midclavicular line, impulse forceful. Sounds of fair muscular quality, with a short localized systolic murmur at the apex. Also a short faint systolic murmur at the aortic area.

Pulses.—Equal, regular, small volume, low tension, vessel walls not felt.

Extremities.—Legs edematous and pale. Knee-jerks equal and active.

Rectal and Vaginal.—Negative.

Lymph-nodes.—Marked enlargement of all the small lymph-nodes; especially the cervical, submental, axillary, epitrochlear, inguinals, and post-cervical nodes; also two posteriorly at junction of neck with thorax, directly subcuticular.

Let us proceed with a further consideration of her physical examination: the striking features are the pallor, the brownish-green color, the purpuric spots on the skin of the chest, the marked enlargement of the abdomen, due chiefly to the large size of the liver, to the much larger size of the spleen, and possibly to a small accumulation of fluid in the peritoneal cavity. A considerable amount of edema in the lower extremities reaching up to each knee is also prominent, and we should not forget the retardation in physical growth which is as dominant and obtrusive as is the distinctly jaundiced conjunctiva. The enlargement of the superficial lymph-nodes in the back and in the axillæ must also be considered.

One's first reaction to these findings in the effort to co-ordinate them into a judgment would be to consider them as indicative of a disease of the hemopoietic system. In order to determine which one of the diseases of that system is present it will, of course, be necessary to ask for the results of the examination of the blood, as that is of prime importance in establishing the existence of one of the hemopoietic diseases. Before asking for that, however, who will volunteer to say what diseases may have the features just described?

Answers: Banti's disease—leukemia—Banti's type of splenic anemia—splenomegalic cirrhosis of the liver with jaundice or Hanot's disease—splenomegalic hemolytic icterus—Gaucher's disease—abdominal form of Hodgkin's disease—pernicious anemia—kala-azar or East Indian splenomegaly.

I think you have assisted me in giving the names to the most of the diseases which could produce the clinical picture which this patient presents.

You will be able to exclude from further consideration some of these diseases by the features already presented and by a

knowledge of one important factor not yet mentioned, viz., the blood examination. Will the house physician give us the result of first the blood-count and then the differential count?

BLOOD-COUNT

December 13, 1923, made by Dr. N. Rosenthal:

Hemoglobin, 30 per cent.

Red cells, 1,520,000—Normoblasts, 9

Color index, 0.98+ Megaloblasts, 8

White cells, 8000 Promegaloblasts, 1

Platelets, 40,000

} Found in field while counting 300 white cells.

Differential

Polynuclears, 22.3 per cent. Lymphocytes, 31 per cent.

Polynuclears (eos.), 0.6 per cent. Monocytes, 0.3 per cent.

Myelocytes (neut.), 10.3 per cent.

Myeloblasts, 5 per cent.

Myelogones, 30.3 per cent.

Are we prepared to give the diagnosis? I think not, even though the blood examination has revealed a marked disturbance in the blood-forming system, particularly in the bone-marrow, which would suggest to the most of you the diagnosis of an active myeloid leukemia; such a diagnosis, of course, is justified by the presence of the anemia, the purpuric spots, the very large size of the spleen, by the presence of the embryonic myeloid elements in the form of myelogones, and the myeloblasts and myelocytes in the blood, and by the existence of the enlarged lymph-nodes, noticeably in the axillæ and in the skin. Even though the white blood-cells are only 8000 per cubic millimeter, the blood-picture as given, together with the physical elements mentioned, would surely justify a diagnosis of a *leukopenic* myelogenic leukemia. You know leukopenia may arise in the course of any leukemia, more commonly in the stage of remission, or it may be a persistent feature of a leukemia from the incipency. In the latter event it is more usually found in the acute variety which is associated with fever, and the signs of an infection, with active hemorrhages from the mucous surfaces and into the skin. The skin hemorrhages then appear as petechiæ, purpuric spots, and ecchymoses. In the acute form

one expects to see in the blood the dominance of embryonal forms of white cells, just as you see in this patient. I don't believe any of you will regard this girl, who has been pale all her life, whose symptoms as noticed by her and her family have been present since July, 1923, who is jaundiced and who has no fever, to be suffering from an acute leukemia. Though the presence of embryonal forms of the *red* blood-cells, the normoblasts and the megaloblasts, the high color index, the anisocytosis, the poikilocytosis, the polycromasia, the macrocytes and microcytes, the large spleen might indicate the existence of pernicious anemia in this girl, such a blood-picture, while uncommon, does occasionally appear in the course of a leukemia, either in its terminal stage or earlier in the disease. Von Leube, who first called attention to the existence of nucleated forms of red blood-cells in the blood in leukemic disease, thought he was dealing with an undescribed form of leukemia, for which he suggested the name of *leukanemia*, believing it was a combination of a pernicious anemia with a leukemia, hence the name.

Those of you who have been following these clinics know that von Leube's disease *leukanemia* is not an entity, for I have repeatedly shown in patients, as have others, that not only may you have the blood-picture of a leukemia in pernicious anemia, but the reverse also occurs, viz., a red blood-cell picture of a pernicious anemia may develop in the course of a leukemia. Some of you may believe that this patient furnishes an instance of the latter. For years I have insisted that when the bone-marrow is actively activated by a general disease which involves it, such activation, if originally confined to the erythroblastic elements such as it is in pernicious anemia, may override the erythroblastic elements and attack the myeloid as well. On the other hand, when the myeloid elements of the bone-marrow are primarily involved in a disease process, such as leukemia, the activation may also affect the erythroblastic elements. This view will adequately explain the presence of myelocytes and their progenitors in the blood of some cases of pernicious anemia, especially during the course of a blood crisis in that disease, as it will equally well explain the not uncommon presence of red

blood primordial elements in the course of a myeloid leukemia. From this point of view there is no justification for the existence of von Leube's disease—leukanemia. What I have just said is most important to remember if you wish to make correct diagnoses. Briefly, then, bear in mind that in cases of pernicious anemia there may be myelocytes and their progenitors in large numbers in the blood, and, on the other hand, in cases of myeloid leukemia there may be many nucleated red blood-cells, normoblasts, and megaloblasts, in the blood with macrocytes and polychromatic cells; in fact, an additional blood-picture of a pernicious anemia.

We do not believe this case is one of pernicious anemia, because of the very large size of the spleen and particularly because of the other blood findings which show a marked increase of bilirubin in the blood and an increased fragility of the red cells as follows:

Bilirubin:	Slight delayed strong direct van den Bergh 1 to 20,000
Fragility of red cells	No hemolysis, 0.7 to 0.6
	Faint hemolysis, 0.575 to 0.45
	Strong partial hemolysis, 0.425 to 0.3
	Complete hemolysis, 0.275

You may ask why this patient then is not an instance of leukemia of the myeloid variety. I do not know that this question can be answered categorically or with absolute certainty. The anemia, the large lymph-nodes, the enormous spleen, the purpuric spots in the skin, and the characteristic blood-picture would all point to the existence of this disease. The leukopenia or, rather, the moderate number of the white blood-cells—8000 to the cubic millimeter—coexisting with the embryonal forms of white blood-cells and the purpura, would suggest the existence of the acute form, which the long history, the absence of fever and other constitutional signs of an acute infection, and the huge spleen which is only present in that size in the chronic form, would deny.

It is not rare that in the course of a chronic leukemia the number of the white blood-cells may markedly diminish and reach finally the number as normally found in non-diseased

conditions; the number may even be reduced to below the normal and a *leukopenia* may result. This is more particularly true since radiotherapy has come into vogue in the treatment of the chronic leukemias—when the spleen is actively radiated in this disease, the white blood-cells rapidly diminish in number in the blood-stream and a leukopenia may thereby be induced.

The high color index and the embryonic type of both red and white cells will at once exclude chlorosis, Banti's disease, splenic hemolytic anemia of Banti, kala-azar, Gaucher's disease, and Hodgkin's disease.

The large liver associated with the large spleen and the presence of jaundice might indicate the existence of that form of splenomegalic hepatocirrhosis which may have been taught to you under the name of Hanot's cirrhosis or hypertrophic biliary cirrhosis, but the blood-picture and the glandular enlargements would militate against such a conclusion, as would the *huge* size of the spleen.

Frederick Taylor, of Guy's Hospital, London, England, some years ago called attention to a disease occurring in children which was accompanied by retardation of growth and infantilism, as likewise did Gilbert and Fournier, in whom liver and spleen were greatly enlarged and in whom arthropathies occurred, and in whom jaundice was a marked feature. This group was considered by him to represent the juvenile type of hypertrophic biliary cirrhosis. This is interesting in this connection because the patient whom we are discussing has a similar retarded development. Retardation in development is not an infrequent accompaniment of the combined hepatosplenomegalies if they develop in childhood, no matter what the form, and has been noted by us in the group which we have called Gaucher's disease, particularly if it develops in early life.

The only condition left to consider is the possibility that the clinical picture in this case is that of a chronic hemolytic icterus. This disease was first described in detail by Minkowski, although there is evidence to cause us to believe that it was known to Murchison who, in 1885, described a family with a disease

characterized by jaundice and large spleen, but without bile in the urine; a member of a subsequent generation was proved by Hutchison and Panton in 1909 to belong to this group. Wilson in 1890 and in 1893 also reported a family with the disease, and had an autopsy on one of the members who died with it. Nevertheless to Minkowski belongs the honor to be the first to describe the disease in detail in 1900. He saw 8 members of a family belonging to three generations, all of whom possessed the same clinical features of jaundice, large spleen, and absent bile in the urine; he had an autopsy on one of these patients who died of an intercurrent pneumonia, in whom there was no evidence of biliary obstruction. The jaundice which evidently was here familial was demonstrated in some of the members of this family to have been present even from birth. It was, therefore, not only familial, but congenital in its nature. The urine in all of them was dark red, contained no bile, and the color was attributed to the presence of urobilin. At the autopsy it was shown that, macroscopically, the liver was normal, the biliary passages were intact, and a bilirubin stone was found in the gall-bladder which, however, had not given rise to any obstruction. The histologic examination of the liver showed no evidence of any pathologic changes which could be considered to be cirrhotic. In the liver cells there was an abundance of pigment which gave no iron reaction. The spleen was said to be hyperplastic and markedly congested; it weighed 1 kg. The kidneys, however, were noteworthy in that they had a brown color due to pigment accumulations which gave a definite iron reaction. Minkowski was able to obtain 0.5 gr. of iron from one kidney alone. He attributed this peculiar disease of liver and spleen to an anomaly in the metabolism of the blood-pigments, and suggested that the disease process might have originated in the spleen.

Levy, a pupil of Hayem, under his teacher's inspiration, published as a thesis a case with greater detail, which had many of the features described by Minkowski, but which had a long-standing jaundice which was neither congenital nor familial. Hayem at first believed that this patient was suffering from a

chronic splenomegalic infectious icterus, as is evidenced by the title of the thesis, "*Thèse de l'ictère infectieux chronique splénomégalique.*" In discussing this case he presents the view that there may have been a bacterial infection of the biliary ducts arising from the intestinal tract, and that the splenic enlargement was the result of a similar infection of the spleen. This patient of Levy-Hayem some years later was further analyzed by Vaquez and Geroux, after the discovery of Chauffard that a marked increase in the fragility of the red blood-cells characterized the disease. They found in this patient a marked diminution in the resistance, therefore an increased fragility of these cells, thus relegating this case to the category of the acquired form of the disease.

The French school, particularly through the work of Chauffard, however, deserves the honor of giving to medical science an exhaustive study of the congenital, familial type of the disease, and through the work of Widal and his pupils the knowledge that, in addition to the hereditary, familial type, there was, chiefly occurring in females, an acquired type of the disease also, whose clinical pictures were almost identical. Widal was able to establish this fact by the utilization of the discovery of Chauffard that a diminished resistance of the red blood-cells was a characteristic feature of this disease. Since their original publications this distinguishing character of the red blood-cells has been attacked. Widal himself presented both congenital and acquired cases of this disease in which there was no diminished globular resistance, and Parkes-Weber and Boulé (a pupil of Widal), Chauffard, and Vincent reported cases in which there was an increased resistance, or diminished fragility of these cells. Therefore both Chauffard and Widal very rightly have since concluded that it is not possible to classify some of these cases definitely, but that it will be wise for the present, because of the etiologic differences and more particularly for purposes of prognosis, which I shall soon bring to your attention, to divide the disease into two forms, viz.:

1. Congenital, familial, hemolytic icterus.
2. Acquired hemolytic icterus.

I may say that it might be desirable to affix parenthetically to the first the appellation Minkowski type; to the second, Hayem type.

As the clinical picture in both types is almost identical it will expedite our discussion to give this picture and to indicate the points of difference. Jaundice is, of course, the prominent symptom. It is a jaundice which exists for years and with varying intensity during the life of the patient. It varies in intensity with the amount and degree of red blood-cell destruction. At times it may be so mild as to tinge but slightly the conjunctivæ, the skin showing no appreciable discoloration; at other times it may be so deep as to be readily observed by the untrained layman. The depth of the jaundice in my experience seems to be greater in the familial than in the acquired type. Nervous excitement or the development of an acute infection may increase the jaundice. Variability in the jaundice is very characteristic of the disease.

Occasionally attacks of colicky pains in the right hypochondrium occur during the intensification of the jaundice; this makes diagnosis difficult because of the likelihood of confusing the disease with cholelithiasis. In this connection one should bear in mind the possibility of such a colic being really due to the presence of a bilirubin stone in the common duct, particularly in view of the fact that in Minkowski's original case a bilirubin stone was found in the gall-bladder. Eppinger had a similar case and so had we. Nevertheless, colicky pains in the hepatic region occur in this disease without the existence of calculi to account for them.

The great distinguishing and important factor is that although jaundice exists, no bilirubin is found in the urine, though in its place is an excessive amount of urobilin. Urobilinuria, therefore, is the important feature. The amount of urobilin in the urine varies directly with the intensity of the disease.

The blood contains an increased amount of bilirubin which may be quantitatively estimated by the test of Van den Bergh and Snapper. They estimate the normal physiologic content of bilirubin in the serum as between 1:400,000 to 1:800,000

dilutions. Their test is the following: having centrifuged some of the patient's blood, the serum is separated. To 1 part of serum 2 parts of 96 per cent. alcohol are added, and the mixture centrifuged. One cm. of the supernatant alcoholic centrifugated serum is added to 0.25 c.c. of Ehrlich's diazo reagent, and on a few minutes' standing the mixture will show a red color. This colored mixture is then colorimeterized against a standard solution of a freshly prepared chloroform solution of pure bilirubin. Dr. Rosenthal and Dr. Kuttner, of our staff, have found that the color resulting from the mixture of the alcoholic solution of the serum to be tested and the reagent and the color of the standard solution do not agree at all in shade, and have modified the test so as to get the exact shade by adding to the standard a mixture of 95 per cent. alcohol 3 parts and of Ehrlich's reagent 1 part, thus permitting of a more *exact* estimation with the colorimeter.

The estimation of the amount of biliary pigment in the serum, as well as that contained in the contents of the duodenum obtained by the passage of a duodenal bucket, is of great importance in all hemolytic diseases, but particularly in this disease and in pernicious anemia, as it is the best means of determining the benefit derived by splenectomy.

The question arises why bilirubin is not excreted by the kidneys if it occurs so abundantly in the blood. This has taxed the ingenuity of many investigators. The most likely hypothesis, proposed by Eppinger, is that in the presence of urobilinogen (which exists in the circulating blood in this disease) the kidney selectively holds back the bilirubin.

So, as we have just said, the important factor to determine in these conditions is the amount of urobilin which appears in the urine and in the stool, in both of which it is enormously increased. That amount serves as an index to the amount of hemolysis which is taking place within the body. This disease is particularly characterized by an enormous increase in the production of biliary pigments. Amounts excreted in twenty-four hours in the feces exceed at times 2 to 3 grams. These enormous amounts of pigment, of course, negative the belief formerly en-

tertained that the icterus in this disease is but an ordinary manifestation of an obstructive process in the biliary ducts. The very dark color of the duodenal contents, very similar to the B. bile which Lyons considers comes from the gall-bladder, and its high pigment value, speak volubly against such a conception.

The spleen in hemolytic icterus may become enormously enlarged, and when so found in connection with icterus should immediately suggest its presence. The size of the spleen varies in the course of the disease, being subject to many gradations. It always increases directly with the increase in the intensity of the icterus, diminishing when the jaundice diminishes. You may also take it as a general rule that those cases of the disease in which anemia is most pronounced present larger sized spleens. Let me here state that the more intense types of anemia are found with the acquired rather than with the familial forms of the disease. On account of the splenic enlargement many of the patients complain of pain in the left hypochondrium. The pain is most likely due to the presence of a perisplenitis which is not uncommonly found when patients with this disease are subjected to splenectomy. Still, one must bear in mind that some instances of the disease occur in which the spleen is but barely palpable at the free costal border. Not all cases have definite splenic enlargement, though it exists in the most, being of splenomegalic type in a few. In the latter the anterior border may be felt to the right of the mesial line of the body and may be traced well below the umbilicus. The spleen removed by splenectomy in one of my cases showed these limits and weighed 2500 grams.

The liver is also considerably enlarged in this disease. Its surface may be felt well below the right costal edge and its consistency is firm. It is usually smooth and not tender, except during the periods of colicky pains in the right hypochondrium which occur in the course of the disease. In 5 splenectomies for this disease I have never seen a liver to be other than smooth, nor have I seen any gross changes indicating the presence of a cirrhosis.

The blood in cases of hemolytic icterus is the tissue which

shows the greatest change. The presence in large amounts of biliary pigment in the serum is constant in both forms. Changes in the red blood-cells and in the white blood-cells, variations in their number, change in the color index, may occur, giving the picture of a pernicious anemia and even that of a leukemia.

Anemia may be of a very mild degree or be a marked feature. A very intense anemia and variations in the white and red blood-cell characters are chiefly to be found in the acquired and rarely in the congenital form of the disease. This furnishes an important diagnostic criterion. While it is possible that in the congenital form only the large spleen and the icterus may be the suggestive factors, there can be no doubt that in the acquired form marked disturbances in the hemopoietic system indicating a terrific activation of erythroblastic and myeloid tissues may give rise to a very dangerous form of disease, suggesting a pernicious anemia or even a leukemia. In the familial form the number of red blood-cells may be not at all reduced or only slightly diminished, and the color may not show any decided pallor; on the other hand, the acquired form is commonly accompanied by a marked anemic pallor, and the number of red blood-cells is always reduced, even in some cases to 1,000,000 to the cubic millimeter. It is in the last cases that the embryonal red blood-cells and primordial white blood-cells appear in the circulating blood. Before splenectomy was introduced the last group was characterized by a particular fatality.

In this connection let me say here that the prognosis varies greatly between the two forms of the disease. It is commonly good in the familial form, the duration of life being little affected by the disease. One patient with this form lived to seventy years. On the other hand, the anemia in the acquired form was a fruitful cause of early death, particularly in the period before the past five years, since which time splenectomy has been found to be a life-saving and curative measure for patients suffering with acquired hemolytic icterus. The familial form is usually very mild; the acquired form runs, in many instances, a stormy course. After this digression let us resume in more detail the blood characters in this disease.

An important feature of the blood in hemolytic icterus is connected with a change in the resistance of the red blood-cells to hypotonic salt solutions. All of you know that the normal red blood-cells are broken up or hemolyzed in the test-tube when distilled water is added to them; the breaking up of these cells may be prevented by the addition of salt to the water. There is a point in the proportion of water added to normal salt solution and red blood-cells at which hemolysis begins; this point in the water salt solution is found with 0.5 per cent. saline solution. When that dilution is used, the solution shows the first visible tinge of yellow, about 1 per cent. of the normal red blood-cells being hemolyzed. Complete hemolysis of these red blood-cells—or 100 per cent. of the normal red blood-cells—occurs with 0.28 per cent. salt solution, at which the tested solution becomes deepest red. Therefore one may say that hemolysis begins a little above 0.5 per cent. and ends a little below 0.3 per cent. of saline solution. The exact figures show beginnings of physiologic hemolysis at 0.48 per cent. and completion at 0.28 per cent. NaCl. If one centrifugalizes blood, removes the supernatant serum, and washes the remaining mass of red blood-cells with normal saline solution, until free from traces of serum, then uses the washed cells for the test, the figures for the beginning and end-point of the hemolysis may be more accurately determined. This effect of disintegration represents the resistance of the red blood-cells to hypotonic salt solution. In hemolytic icterus the resistance of the red blood-cells is constantly diminished with but few exceptions. If put into figures it will show that hemolysis of the red blood-cells in hemolytic icterus begins between 0.66 and 0.55 per cent. of saline, and is complete before 0.3 per cent. is reached; if one uses the washed-cell method hemolysis begins not infrequently at 0.9 and ends at 0.4 or sooner.

Another remarkable phenomenon that seems to be peculiar and limited to these groups of hemolytic icterus is that of auto-agglutination. If normal washed red blood-cells be added to the normal individual's serum in a watch-glass, or on a glass slide, they sink to the bottom as individual and separated cells. If, however, the test be made with the washed cells and the

serum, both derived from the blood of a patient with hemolytic icterus, the cells instead of being perceived as distinctly individual will be agglutinated into a compact homogeneous mass. It was supposed originally that auto-agglutination occurred only with the blood of the acquired hemolytic icterus group and not with that of the familial form, but that does not seem to be true; nor is the test demonstrable in more than a small number of the cases of the acquired form of the disease.

It is much more important to rely upon the increased fragility or, as we have just called it, the diminished resistance, than upon the auto-agglutination test in determining the presence of this disease.

The presence of large numbers of reticulated red blood-cells is very common and is particularly marked in the acquired form. To those of you who read German literature reticulation of the red cells will be revealed to you there under the name of *substantia reticulofilamentosa*, *substantia filamentosa granulosa*, or *filamentöse Granulierung*; in French literature, as *hématies granuleuses*. The best method to find these morphologic immature red blood-cells is to add a drop of alcoholic brilliant cresyl solution to the glass slide and then add a drop of the blood and cover the mixture with a cover-glass and examine under the microscope. However, I hold that reticulated red blood-cells occur in various forms of severe anemia, and their presence is not diagnostic of this disease; that they do not indicate, as Chauffard believed, the physical expression of cells whose resistance is diminished, because they are commonly found in cases of pernicious anemia in which disease the red blood-cell is very resistant and much less fragile than even the normal red blood-cell.

In the blood of hemolytic icterus cases and particularly in that of the acquired form, anisocytosis, poikilocytosis, nucleated red blood-cells, and polychromasia are commonly found. In a few cases the color-index may be more than 1. Parkes Weber has called particular attention to the blood-picture of some cases of acquired hemolytic icterus as being that of a pernicious anemia. In such cases the increased fragility of the

red blood-cells in the former would differentiate the condition. There is no doubt in my mind that the diagnosis of pernicious anemia has been erroneously made by clinicians in some cases of this disease, and reported as cures of pernicious anemia following splenectomy.

When we come to speak of the pathogenesis of this disease we shall see that it is the result of a tremendous destruction of the red blood-cells of the body; that the hemopoietic system is called upon to replace these destroyed red blood-cells, the oxygen carriers for the needs of the essential metabolism of the tissues, and that this terrific activation of the hemopoietic system calls forth bone-marrow excitation, which finds its expression in early forms both of red blood-cells and white blood-cells. Hence myelocytes frequently appear in the blood, particularly in those cases of serious anemia which commonly attend the acquired form of the disease. Not only are myelocytes present, but they may be so in large numbers, as may their progenitors—the myeloblast and myelogone. Both Blumenthal and Eppinger have described such cases as simulating the blood-picture of a myeloid leukemia. I was asked to see a patient on the pediatric service six months ago who had hemolytic icterus of the acquired type with a leukemic blood-count, there being 15 per cent. of myelocytes in the blood. Gaisböck has reported one case of this disease with the blood-picture of a lymphoid leukemia. While no other observer has seen a case with the latter blood-picture, for the present it must be held as a very unique observation. Possibly Gaisböck's lymphocytes were primitive myeloblasts and myelogones. When we analyze the blood-picture of our patient here you will find that it is one possessing in addition to the characters of a hemolytic icterus, prominently those of a myeloid leukemia, as well as those of a pernicious anemia.

As a rule in cases of hemolytic icterus, except in the rare forms accompanied by excessive bone-marrow activation, there is neither hyperleukocytosis nor hypoleukocytosis. In fact, an intense leukopenia is not found in this disease, and if present ought to suggest some other diagnosis, such as a splenomegalic hepatic cirrhosis.

The feces in cases of hemolytic icterus are always highly colored; they are never free from pigment. They contain an excess of urobilinogen and urobilin greater than that found in any other disease. There is more urobilin in the urine and feces of the acquired than is found in cases of the familial form of the disease.

A few cases have been found in which hemolysis has been so excessive as to have produced a hemoglobinuria. Hemoglobinuria, however, is a very rare accompaniment of the disease, there being but 5 cases on record.

The pathogenesis of this disease seems to be found in the spleen. This is evidenced by the results of the removal of the spleen in these cases. The icterus disappears, the bilirubinemia approaches the normal, the anemia vanishes, and the blood-picture returns to approximately normal. The improvement in the patient's condition is remarkable, and one may say that splenectomy cures the disease.

When the spleen thus removed is examined it is found to be large, the increase in size being due chiefly to a massive accumulation of blood within the organ. On cutting the viscus blood flows freely from the cut surface. It gives the appearance as if the entire spleen were like a huge fresh infarct. So rich is the spleen in red blood-cells that its structure cannot be defined, the malpighian bodies being indiscernible. Eppinger explains this abnormal fulness of the spleen with blood as due to an abnormal deflection of the red blood-cells by the disturbed reticulo-endothelial system in the spleen, diverting the cells to the open spaces from the closed vascular channels. Here the red cells are prepared for their ultimate hemolysis in the Kupfer cells of the liver, furnishing more bile-pigment than can be utilized and producing at the same time not only a polycholia, but an abnormal change in the consistency of the bile, a pleiocholia, resulting in the icterus which is one of the prominent signs of the disease. Thus we see that this disease involves the whole reticulo-endothelial system, particularly that of bone-marrow, liver, and spleen.

With this summary of the disease let us apply its characters to this girl, the patient under discussion.

She has a very intense anemia, a large liver, a huge spleen, and she is definitely and decidedly jaundiced; her urine contains no bilirubin, but large quantities (85 milligrams) of urobilin; her stool is very dark brown in color and also contains an excessive amount (1.2 gm.) of urobilin. Her blood-serum contains much bilirubin—1:20,000. The microscopic examination of her blood in addition to the characters pointing to a pernicious anemia and to a myeloid leukemia, previously brought to your attention, shows a marked anisocytosis and poikilocytosis and polychromasia, many microcytes, and 5 per cent. of all the red blood-cells are reticulated.

The tests for the resistance of the cells shows that that quality of the cell is markedly diminished, hemolysis beginning at about 0.6 per cent. hypotonic salt solution.

Therefore we cannot help concluding that this girl is suffering from an acquired form of hemolytic icterus. We might even regard her exceptional blood-picture, indicating an intensive myeloid activation, as an exceptional feature of her disease, though nevertheless a part of it. Still one must bear in mind that no case has ever been reported with the extreme adenopathy which she presents and with a white blood-count in which myelogones were the predominating cell. Therefore a diagnosis of myelogenic leukemia would be justifiable; but that disease in this case can be looked upon only as a concurrent affection, and not as the dominating and only existing disease, because jaundice does not occur in leukemia of any type except as an agonal phenomenon, nor do the red blood-cells show increased fragility, nor do the urine and stool contain increased amounts of urobilin. Therefore, as I said earlier in this clinical lecture, it is quite possible that we are dealing with an incidence of two co-existing diseases, namely, that of an acquired hemolytic icterus and of a myelogenic leukemia, or that possibly the blood-picture which indicates the existence of a leukemia may be due to a myeloid activation of a degree not yet described as occurring with hemolytic icterus. The suspicion that there is a

concurrent leukemia is supported by the microscopic appearance of one of the lymph-nodes which we had excised, which is that of a myeloid metaplasia with mitotic cells.

The most important factor in reaching a conclusion as to the dominating disease present in this case is the retardation in the physical development of this girl. The short stature, the childish expression of countenance, and the absence of pubic hair demonstrate this defect. As I said before, retardation in growth is not uncommon in diseases affecting the hemopoietic system, when such disease develops in childhood. Particularly is this true in the cases associated with splenomegaly. This girl has been "pale as long as she can remember," which is evidence of the existence of some disturbing factor present since childhood in her blood-forming organs. This retardation is the expression of the effect of a chronic disease, which hemolytic icterus is. It is most probable that her disease followed infection by one of the exanthemata which occurred in her early life. Retardation in growth has not been reported as occurring in the course of a leukemia. Therefore we may assume that she has had hemolytic icterus in the acquired form since childhood, and that the leukemic blood-picture is a secondary and much later feature.

What shall we do for this patient? If she be suffering from an acquired hemolytic icterus, there is a curative agent at our command—splenectomy. There is no use in attempting x-ray treatment of the spleen in this disease because in our experience it is absolutely valueless; it is neither palliative nor curative. If used it makes subsequent operative interference only more difficult on account of the production of adhesions, and attended, therefore, by increased risk.

If the case be one of myelogenic leukemia the patient will surely die quickly, even without operative interference. Therefore, as nothing would be lost by splenectomy even in the event that this were a case of myelogenic leukemia, and as she might be restored to health and economic productiveness by the operation if it be a case of pure hemolytic icterus, I shall advise her family to have her submit to the operation, and will report

to you the results of the surgical procedure at a subsequent clinic. I shall recommend, however, to the surgeon to transfuse this patient immediately before and, if necessary, immediately after the splenectomy.

Medical Clinic, January 23, 1924.—Gentlemen: Permit me before proceeding to the presentation of the new clinical material which shall engage our attention today to show you the patient with the leukemic blood-picture attending upon the presence of a hemolytic icterus. You may remember she was the subject for discussion just four weeks ago. At that time I told you that we would have a splenectomy performed in the hope that if the case proved to be one of hemolytic icterus the operation would cure her disease; that it was the only chance left for her in view of the fact that if the leukemic blood-picture indicated the presence of an additional leukemia, that disease would necessarily be fatal. I stated to her parents that she had everything to gain by the operation, and that she would die unless it were done.

On December 29, 1923 Dr. A. A. Berg performed a splenectomy, preceding the operation by a transfusion, and following it immediately by another transfusion. The spleen was delivered (fortunately there were no adhesions of the organ to neighboring structures) and removed in less than six minutes. It was monstrous in size and was found after removal to weigh $5\frac{1}{2}$ pounds. Its subsequent examination by our pathologist, Dr. F. S. Mandlebaum, showed a myeloid metaplasia with mitotic cells in addition to the characters of a hemolytic icterus spleen.

You see the patient now remarkably improved; she has practically lost her jaundice, her conjunctivæ are no longer tinged, her cheeks and visible mucosa are red, she has gained 9 pounds in weight, and she is able to walk about.

On the next day after the splenectomy the hemoglobin, which had been 30 on the day before the operation, rose to 62, mostly on account of the transfusions, and her red blood-cells rose to 2,500,000. The blood-picture up to the day before yesterday was as follows:

Hemoglobin—varied between 60 and 65.

Red cells—2,500,000; white cells increased from 8000 to 12,500.

Platelets—increased to 120,000.

Polymorphonuclears—increased from 22 to 67 per cent.

Myelocytes—increased from 10 to 22 per cent.

Myeloblasts—not influenced.

Myelogones—decreased from 30 to 2 per cent.

Monocytes—unaffected.

Normoblasts—increased from 9 to 20, then diminished to 13 (found in the fields while counting 300 white cells).

Megaloblasts—increased from 8 to 77, then diminished to 26, and finally to 3 per 300 white blood-cells.

Blood bilirubin decreased from 1:20,000 to 1:100,000. Urobilin in twenty-four hours decreased in urine from 500 to 106 milligrams in two days after splenectomy.

The lymph-nodes have also diminished in size. One would think that this improvement indicated the leukemic picture was but an accompanying phenomenon of the hemolytic icterus. Still I cannot even now deny the possibility that the patient has the two diseases; this view the future will have to decide. If she is suffering from an additional leukemia the removal of the spleen will not cure her and her duration of life will be but a few weeks.

Since the clinic of January 23, 1924 was reported, the patient who showed signs of remarkable improvement after the splenectomy died. The improvement lasted about one month. Her white blood-cells began to increase in number, reaching over 100,000 per cubic millimeter. And her lymph-nodes, which had at first receded in size, took on renewed increase. The jaundice did not return, the bilirubinemia diminished, and bilirubin in her blood-serum was present in normal amounts. Urobilin in the urine was present only as a trace. The red blood-cells became less fragile. The disappearance of her jaundice, of her bilirubinemia, and of her urobilinuria indicated the disappearance of her dominant disease, *chronic acquired*,

hemolytic icterus. At first we regarded the large increase in the number of her white blood-cells as the usual expression of reaction of the myeloid tissues to the removal of the spleen. Hyperleukocytosis always follows a splenectomy and may exist for some weeks after the operation, but the continual presence of primitive forms of white blood-cells in the blood of the patient, the increasing size of the lymph-nodes, the reduction in the number of the red blood-cells, an increasing pallor and weakness, a return of the edema of the legs and a reappearance of epistaxis, bleeding gums, and of hemorrhages into the skin indicated the existence of a leukemia which caused her death. An autopsy confirmed its existence. This was proved by a myeloid transformation of the lymph-nodes, leukemic cellular infiltration in the liver and kidneys.

This case, therefore, of a combination of chronic acquired hemolytic icterus and myeloid leukemia is the only one recorded up to date in the literature.

CLINIC OF DR. BURRILL B. CROHN

MOUNT SINAI HOSPITAL

THE CONSERVATIVE TREATMENT OF HOUR-GLASS STOMACH

THE statement that an hour-glass deformity of the stomach exists in a given case, particularly when an ulcerative lesion of this organ is conjectured, gives rise instantaneously to the thought that surgical intervention must sooner or later be invoked. And not without reason, for this condition constitutes one of the most vicious of the mechanical deformities resultant from peptic ulcer, or from cancer or syphilis invading the body of the stomach. The very nature of the lesion, a mechanical one, seems immediately to invoke an equally mechanical means—surgery—for its abolition.

The following 2 cases are, therefore, all the more instructive, in that definite and lasting improvement in the clinical course was brought to pass by the simpler, safer, and more conservative methods of internal medical therapy.

Case I.—An unmarried woman, thirty-four years of age, had suffered for fifteen years with vague abdominal symptoms. She complained of pains, sticking or pressing in character, localized in the epigastrium and referred to the left hypochondriac segment, and around to the left border of the dorsal region of the trunk. The pains were worse after eating, coming on almost immediately after partaking of food. They were accompanied by belching and the eructation of gas. There was no relief afforded by alkalies. There was, however, complete relief created by the act of vomiting; vomiting was either spontaneous, occurring about once a week, or on other occasions when the distress was overbearing, emesis was self-induced, with equally great satisfaction. The bowels were costive. A loss of weight of 25 pounds had taken place gradually over the course of the last few years, most of the loss, however, having occurred in the recent months. Of her own accord she had restricted her diet to a considerable degree. Her dietary habits were poor, however, food being taken irregularly and without much discretion or judg-

¹ From the Medical Department of Mt. Sinai Hospital.

ment. The patient was not nervous or excitable, being a descendent of the Nordic races and inclined to phlegm and complacency rather than to temperamental irritability.

The physical examination revealed a woman rather of the enteroptotic build, narrow epigastric angle, broad flare of the false pelvic basin. There was an evident loss of subcutaneous fat. The teeth and tonsils were apparently free of disease. The examination of the chest proved negative. Abdominally, physical signs of disease were absent. The abdominal walls were relaxed, there being no tender areas or masses to be felt. The sigmoid colon could be palpated as a spastic loop of intestine. The peripheral reflexes were all present and equal. The patient was distinctly subsensitive to pain, firm pressure upon the styloid process anterior to the mastoid prominence (Libman's test) failing to elicit a painful response.

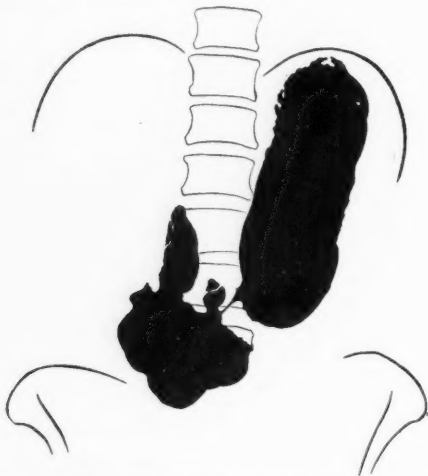


Fig. 35.—Silhouette of hour-glass deformity of the stomach of Case I.

The Wassermann reaction was reported as being completely negative.

A fractional test-meal showed a small amount of fasting secretion free of evidence of food residue. The acid curve was fairly high, but was quite in accord with the type of hypersecretory curve classified by Rehfuess as within the upper limits of normalcy. The emptying time of two hours on an oatmeal gruel test of 500 c.c. was quite within the average range of gastric motility.

A Roentgen-ray examination (February 3, 1923), both fluoroscopic and by plate, revealed a stomach which was long, situated vertically, and somewhat ptosed. The tone of the organ was good; peristalsis was irregular in depth and frequency. The lower pole, with the patient in the erect position, reached about 3 inches below the level of the crest of the ileum. Situated on the greater curvature opposite the re-entrant angle was a deep indentation of

the contour which extended almost to the lesser curvature and divided the stomach into two unequal pouches, giving it an hour-glass appearance.

With the ingestion of the barium mixture the food immediately filled the upper pouch. After an interval of about five minutes some of the food was seen going through a narrow irregular canal about $\frac{3}{4}$ inch long which was situated along the lesser curvature and communicated with the lower pouch. Gradually the latter portion of the stomach filled up. As the lower pouch became full the food began to pass out of the pylorus and filled the entire duodenum.

Motility of the stomach was obviously delayed. At an observation made six hours after the ingestion of the opaque meal about one-half of the meal was still present in the stomach, being all within the lower loculus. At the twenty-four-hour observation a very small residue was still present in the lower gastric chamber. Intestinal motility was not abnormal.

The Roentgen-ray examination indicated the presence of an ulcerative lesion of the lesser curvature at the re-entrant angle, or *incisura angularis*, the lesion giving rise to an hour-glass deformity of the viscus. As one conceives of the formation of such a lesion one necessarily pictures an ulcer of long standing which had undergone a slow chronic penetration into a neighboring viscus, usually the liver. As the perforating ulcer fixes itself against this greater body it uses this as a point of support and throws out connective-tissue trabeculae and adhesions which span the circumference of the ventricle of the organ. As these latter contract they cause retraction of the opposite wall of the viscus, thus mechanically reproducing a deformity similar to the hour-glass of the ancients.

Having determined the latter is only half the task, for one has still to consider the various etiologic factors and disease which can give rise to such a clinical deformity. Far and above all in frequency is simple benign callous peptic ulcer. Hour-glass deformity constitutes a stage, often a late stage, in the life-cycle of ulcer. It often represents the final or cicatricial end-result of an ulcer which has run its course, one which in its remote healing phase has included in its scar the body of the organ with a resultant constriction of its lumen by scar tissue. A true organic hour-glass deformity rarely if ever accompanies an active bleeding ulcer, but always a penetrating lesion. An ulcer in its earlier stages burrows deeply into the

walls of the organ, seeking its depth. As it completes its invasion and makes of a neighboring organ its bed, it has a more natural tendency to cease its attempts to penetrate and now grows by extending its periphery in the form of an advancing wall of callous indurating tissue. This, too, eventually ceases. Scarring and scar-tissue contraction now produces the mechanical deformity and end-result, be it a "cascade" form of stomach in the fundus, an hour-glass deformity of the ventricle, or a stenosis at the pyloric outlet of the viscus. Each in itself constitutes a late or an end stage.

Carcinoma, particularly of the scirrhus type, that in which the connective tissue far exceeds in bulk the malignant cellular component, is prone to reproduce hour-glass deformities. As the neoplasm extends it seeks the circular lymph canals that extend in parallel and closely knit channels about the body of the organ in its serous covering. In this manner an encircling collar of neoplastic tissue may create and reproduce the condition similar to benign scar tissue hour-glass deformity. Malignant hour-glass is said by Carman to constitute less than 1 per cent. of all such deformities.

Next in frequency to peptic ulcer stands lues as a disfiguring factor, syphilis in the form of a diffuse gummatous infiltration of the gastric walls. Connective-tissue infiltration is a pronounced element in syphilitic processes; in its later stages, therefore, lues may play quite a rôle in reproducing an organic biloculation of the ventricle of the stomach.

Certain individual mechanical characteristics differentiate the various types of deformities caused by these three factors. Thus, in benign hour-glass the two chambers are usually of decidedly unequal proportions, the upper, as in the case cited, being more voluminous than the lower. The neck or isthmus connecting the two loculi is narrow, the walls of the indentation being steep and smooth, but approaching each other by a sharp acute angle.

In the malignant hour-glass, on the other hand, the loculi are more inclined to be of equal magnitude, since such carcinomata more frequently arise on the posterior wall, the "silent

area" of the stomach, and extending in a circular, but wider and more diffuse manner, cause a broad collar-button-like constriction of the lumen approximately in its middle stretches.

Luetic hour-glass deformity is more generally a diffuse invasion of the submucosa by gummatous infiltration. It gives an appearance similar to the letter X. The isthmus is broad, ill defined, the walls vague in outline, the connecting lumen irregular, often devious. The serologic reaction and the often favorable response to antiluetic therapy distinguish it without particular difficulty.

Apart from the consideration of organic disease processes which can create such a deformity one must pause to investigate the factor of muscle spasm as a cause or an incident to such a functional contracture. This evidence of functional hyper-irritability on the part of the neuromusculature of the stomach is met with in a large group of cases which we correlate under the name of spastic hour-glass stomach.

In the latter we distinguish two forms—those due to intrinsic and those due to extrinsic lesions of the stomach. By far the most common intrinsic cause is an ulcer, usually an ulcer on the lesser curvature, and very often a penetrating one with a well-defined niche.

The ulcerative process gives rise to marked spasm of the greater curvature at a point opposite the ulcer. The contralateral border is thus retracted and drawn in toward the ulcerated surface in a constant and unremitting spastic contracture. Such a functional hour-glass is only distinguished with difficulty from a true hour-glass, in which scar tissue and not nervous spasm is the controlling element.

Of the extrinsic causes of spastic hour-glass authors are prone to quote gall-bladder disease, duodenal ulcer, chronic appendicitis, renal calculus, and pure nervous spasm due to exaggerated vagotonic or psychasthenic state. Of these various causes cholelithiasis and duodenal ulcers are the most frequent offenders.

In the particular case under discussion the history would seem to indicate the presence of a healing or healed gastric

ulcer at the incisura angularis. The active symptoms of ulcer have pretty much subsided. Upon closer analysis of the complaints one sees that the vague distress and discomfort after eating are due more to the mechanical difficulties of the food passing through the narrow neck connecting the loculi rather than to the ulcer itself.

One further observation is of interest. Practically every hour-glass stomach we have observed has occurred in a person who is subsensitive or insensitive, as tested with pressure over the styloid process. This point has value, since it explains why it is that these patients complain so little during the long active course of the ulcer. They often come under observation of the physician for the first time with the evidence of a late complication and not of the ulcer itself.

For instance, this insensitive woman had never been treated for her gastric complaint, though upon closer questioning she admitted to postprandial pains and discomfort for fifteen years. It was only the recent mechanical difficulty of swallowing food and loss of weight that made her seek the advice of a physician. Any indication of a nervous excitability or of a spasmodic element to this hour-glass seemed lacking.

In spite of the fact that mechanical deformity was present and notwithstanding the radiographic evidence of six-hour (even slight twenty-four-hour) delay in gastric motility, it seemed warrantable to try the effect of medical treatment for the ulcer. This was undertaken, with the view that perhaps *after all* a part of the hour-glass was spastic and functional.

The patient was put to bed in the hospital and given a modified Sippy diet. Not doing very well upon this diet, owing to considerable abdominal gas and distention, a complete change was made. As is our custom, oatmeal gruel was substituted for the milk, 3 to 4 ounces being given every hour for two days, then gradually increasing amounts of the gruel until 6 ounces were given every two hours. Other, more solid, cereals were next given, and gradually an egg, puréed vegetables, and stewed fruit added. Rest in bed was enforced for at least two weeks and considerable physical relaxation insisted upon for a still

longer period, up to one or two months. Small doses of alkaline powders were administered, though never in the same large dosage or frequency which Sippy recommends. Tincture of belladonna was prescribed up to full physiologic effect and continued for several weeks.

The effect of the diet was a beneficial one. The few symptoms of distress after meals disappeared rapidly. The patient felt well and began to gain weight and seemed to think that the diet was all sufficient for her needs. She reported at intervals after this. There was a steady gain in weight. Within the first two months there was a gain of 10 pounds, and within the succeeding three months a further increase of approximately 14 pounds. She was free of all symptoms.

The re-examination of the patient roentgenographically seven months after she had come under observation rather surprisingly showed the same condition as upon the original radiograph. There was no direct evidence of ulcer, but there was definite hour-glass contracture practically identical in its shape, form, and magnitude as upon the earlier examination. There was, however, better function, there being no six-hour residue in either the upper or lower loculus, food passing through the isthmus quite freely. It is therefore apparent that while no change in the organic structure of the stomach had been effected, a functional benefit in the form of relaxation of the spasmodic element was apparent.

The improvement and benefit accruing to this patient remains to date, though no further gain in weight has taken place. There has been no change in her dietary regimen; meat is still excluded. There is every reason to hope that this improvement will be a lasting one. Presumably the mechanical scarring in the stomach has become non-progressive; the present status is probably its permanent status. The spastic element, under proper diet and with belladonna administered intermittently at long intervals, seems sufficient to counteract the functional spasm. The rest in bed and the diet probably to a much greater degree than the atropin seem effectual factors in bringing about this unexpected good result.

Case II.—The following case is one cited as having many marks of similitude with the preceding one, but again as one having features characteristically its own.

A married woman, thirty-eight years of age, gives a history of having suffered for fourteen years with epigastric pains and "indigestion" immediately after partaking of food. The pains are worse when she walks—exertion of any kind gives rise to cardiac palpitation. There has been no history of vomiting. The bowels have been markedly constipated. She has lost 22 pounds in weight in the last few years, weighing at the time this history was first taken only 95 pounds. She sleeps poorly and admits to a certain degree of nervousness.

The physical examination shows a woman of large frame in a state of malnutrition. There is a very evident exophthalmos; both Graefe's and Moebius' sign are present. The pulse-rate is 102 per minute; she flushes easily and has a slight but distinct tremor of the hands. The peripheral knee reflexes are not increased and the test for sensitiveness (Libman's test) over the styloid process shows, in spite of the evident state of autonomic imbalance, a subsensitive index to pain.

The radiographic examination of this patient showed a stomach vertically situated, extremely ptosed, the lower pole reaching $5\frac{1}{2}$ inches below the crest of the ilium. Situated on the greater curvature, midway between the pylorus and the cardiac opening, is a broad incisure which extends to the lesser curvature and divides the stomach into two pouches, giving the stomach an hour-glass appearance. Running along the lesser curvature and connecting the two pouches there is a narrow canal about $2\frac{1}{2}$ inches long. There is also a suggestion of a small penetration on the lesser curvature just above the incisure. The duodenal bulb is regular in contour and not tender. The motility of the stomach was not delayed.

Apparently we were dealing with a condition very similar to that of the preceding case. If this is an ulcer with an organic cicatricial hour-glass stomach, then the fourteen years of independent epigastric pain and slight discomfort was the sole evidence of the activity of such a process. Either the ulcer is a small superficial one, not penetrating deeply enough to expose the sensory apparatus in the plexuses of the ulcer, or it has progressed in so indolent a way as to give rise to none of the indirect manifestations of its presence, such as gastric spasm, hyperacidity, hyperperistalsis, etc. The third requisite would be a patient who is so insensitive to pain that she neither feels nor complains of afferent pain stimuli which in the ordinary individual would mean a complete "ulcer" symptom-complex.

In considering these three possible factors we must immediately exclude the first, for it is hardly likely that an ulcer which

is too superficial to give marked symptoms could give a scar-tissue contracture. After all an hour-glass stomach is a disease or contracture of the peritoneal covering, for the mucosa heals without a scar as well as the submucosa. It is only when the deeper muscularis and the serosa are involved that permanent cicatrization is induced.



Fig. 36.—Biloculation of stomach in Case II. Note the tendency of the upper sac to overhang the lower sac. Small penetration seen on the lesser curvature is the probable site of an ulcerative lesion.

We must, therefore, conceive an hour-glass stomach as being created by a deep penetrating lesion continuing over a course of many years and taking place in a patient whose involuntary nervous system does not react actively to an ulcerating process (secretory and motor functional disturbances), and second, one whose cerebral receptive areas are subsensitive to painful stimuli.

We have often noted that, as a rule, an acute perforation of peptic ulcer takes place in a patient who is markedly subsensi-

tive. Not at all infrequently the perforation is the first sign of the presence of the ulcer. On cross-examination one may persuade the patient to confess to having had for a few days or a week or two mild indigestion, slight belching or a little fullness after meals, symptoms which might well be present in any normal individual without giving rise to any suspicion of disease. Here again is a class of phlegmatic persons who are unconscious or insensitive to all the manifestations of their ulcer until it perforates. If such an ulcer, instead of perforating, becomes ad-

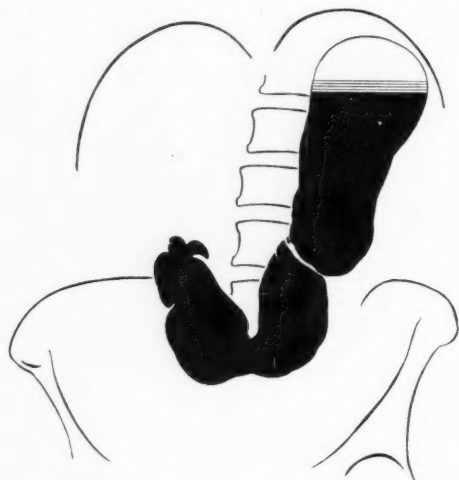


Fig. 37.—Same case after rather prolonged medical treatment.

herent to neighboring organs and smoulders for years and years, then an hour-glass deformity may result.

In this second case under discussion we have the one other factor of a fairly clear exophthalmic goiter—Basedow's disease. It is rather peculiar to find this combination of autonomic imbalance with its flushing, perspiration, tremor, and loss of weight, and, on the other hand, this state of subsensitiveness to pain, and yet both conditions are present in this patient.

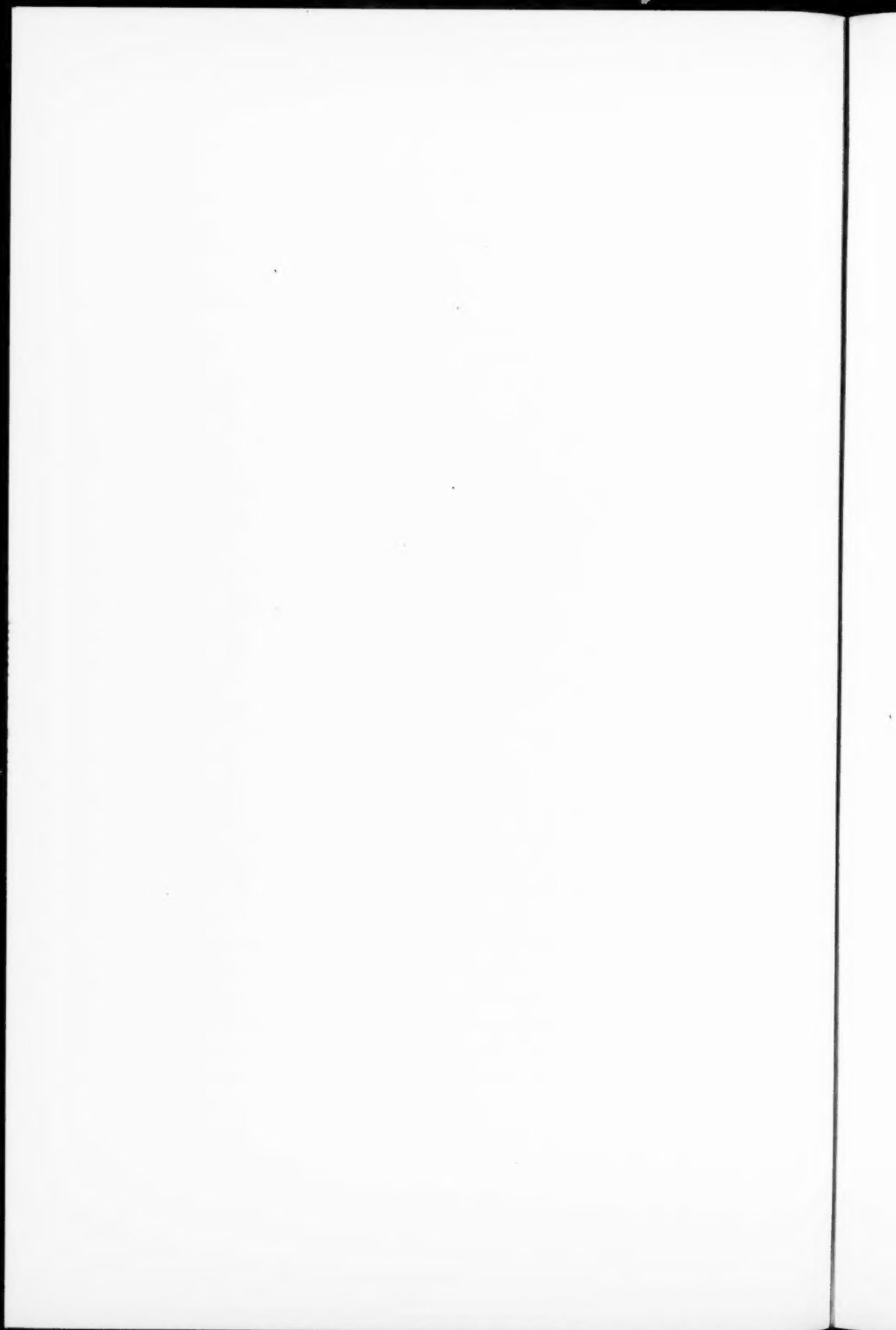
To what extent is this hour-glass a purely spastic or functional phenomenon? The course of the case under observation

would seem to deny this hypothesis. Without making any radical change in this patient's daily habits, she was directed to eat five times daily, small amounts each time, to balance her diet by the exclusion of coarse fruits and vegetables and roughage. The diet was concentrated; the main emphasis being laid upon milk, eggs, cereals (well cooked), puréed vegetables, fruit juices, etc. Meat extracts, finely divided and well-cooked meats, were gradually added. Fats, in the form of a proprietary emulsion of oils, was prescribed in an attempt to increase her weight. The result of this treatment was a rapid and almost continuous gain of weight, with a subsidence of all (that is those few) abdominal symptoms which had previously been present. In six months there was a gain of 33 pounds. The exophthalmic symptoms were still present, though not very marked.

A re-examination of the stomach at this point roentgenographically showed the deformity of the stomach to be present to an unaltered degree. There has been very little change except for the fact that the upper loculus has somewhat contracted and no longer overhangs the lower chamber to the same degree as on the previous examination.

An hour-glass deformity which is so constant that it is still present after six months of well-being, clinical improvement, gain in weight, and freedom from abdominal complaints cannot conceivably be called a purely functional or nervous gastropasm, for the latter vary considerably in size and position, and its occurrence is never constant. It would undoubtedly have disappeared in the presence of such a marked clinical change for the better.

These 2 cases indicate the fact that not every hour-glass stomach is necessarily an immediate surgical risk. Such a deformity is evidence of a spent process, one in which the fire has practically died out, and left a permanent mechanical change. If the mechanical deformity has stopped at a point before complete obstruction to the passage of food has ensued, then the case may still remain a medical problem, one in which much benefit may accrue by conservative and cautious treatment.



CLINIC OF DRS. ERNST P. BOAS AND PHILIP RIFKIN

MONTEFIORE HOSPITAL FOR CHRONIC DISEASES

THE HEART IN CHRONIC MULTIPLE ARTHRITIS

WE wish to present in this clinic a number of cases of chronic multiple arthritis (arthritis deformans), laying emphasis on the cardiac lesions which these particular patients exhibit, and discussing the relationship between the heart disease and the arthritic disorder. There is so much confusion and uncertainty concerning the classification of chronic joint disease that it is essential to define the types of cases that we have studied. We have followed McCrae in designating as chronic multiple arthritis or arthritis deformans "the group of cases of arthritis which have as prominent features a tendency to chronicity and to more or less permanent change in the joints or structures about the joints, those forms of arthritis with a definite etiology being excluded." We have termed the onset "acute" when evidences of arthritis, namely, pain, tenderness, limitation of motion, swelling of the joint, with or without fever or constitutional symptoms, developed suddenly or within one week in one or more joints; "subacute" when the signs and symptoms developed in the course of two months; and "insidious" when the joint disorder became slowly manifest in the course of months or years.

A study of these cases will lead us to a general survey of the subject of the nature and frequency of cardiac involvement in chronic deforming arthritis.

Case I.—Arthritis deformans; insidious onset; aortic insufficiency.

R. G., aged fifty-six; female; married. Admitted May 13, 1921, complaining of pain and limited painful motion in various joints, inability to walk and general weakness.

Family history negative.

Past History.—Married at eighteen years. Eleven pregnancies; 8 children are living and well; 1 still-birth; 2 children died in infancy. Menopause at fifty. Otherwise past history negative.

Present Illness.—Began at about forty years of age with pains in right wrist-joint. Gradually, in the course of many months, the joint became tender, swollen, and ankylosed. At intervals of months and years other joints became gradually involved in about the following order: left knee, left elbow, right knee, spine, and other joints. These joints gradually became swollen, tender, deformed with limited motion, so that a few years ago patient became chair-ridden and quite helpless. Her heart condition was first



Fig. 38.—Left hand of Case I showing advanced arthritis, especially of carpus.

noticed on admission to this hospital. During the last few years patient has had moderate dyspnea on exertion, occasional precordial distress and palpitation, but no edema and no coughing. The course of the polyarthritis was, in general, progressive, afebrile, with periods of quiescence of variable duration. Nine years ago all teeth were removed, but the course of the arthritis remained uninfluenced.

Physical Examination.—Fairly developed and well-nourished elderly

female of short stature, chair- and bed-ridden. Head negative, except for absence of all teeth. Chest: Heart moderately enlarged to left and right. Action, regular, rate 90 per minute; aortic diastolic and systolic murmur at base, the systolic transmitted along large cervical vessels; the diastolic transmitted to left sternal border and to apex. A systolic and diastolic murmur are heard at the apex. Arteriosclerotic changes in peripheral arteries slight. Blood-pressure varying from 160/90 to 110/70. Lungs and abdomen: Essentially negative. Lymph-glands not enlarged. Marked arthritic changes involving joints of all extremities and also temporomandibular joints and part

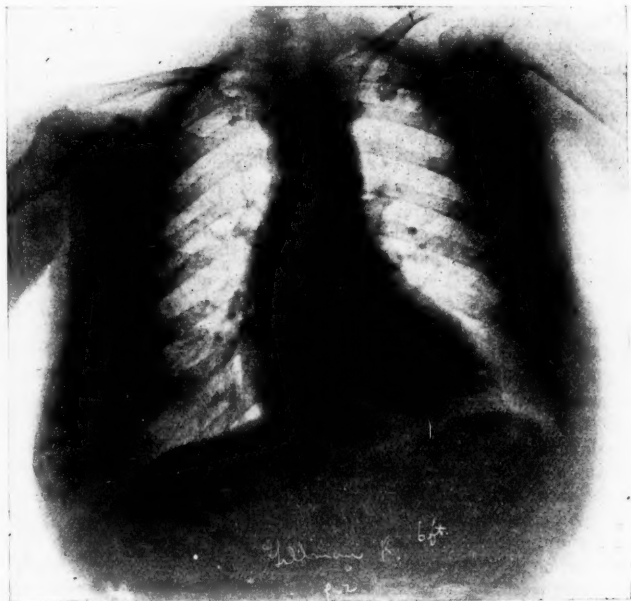


Fig. 39.—Teleoroentgenogram of Case I showing enlargement of all chambers of heart.

of spine. Marked hard periarticular swellings with some tenderness and marked deformities. Motion limited from complete ankylosis (both wrist-joints) to moderate limitation of motion (in both shoulders). Reflexes and sensory negative.

x-Ray of joints shows advanced polyarthritis of hypertrophic type (Fig. 38).

x-Ray of heart shows heart slightly enlarged both to right and to left. Its dimensions are: M. R., 5.8; M. L., 10.7 (Fig. 39).

Laboratory data: Blood Wassermann, urine and blood chemistry negative.

Case II.—Arthritis deformans; acute onset; mitral stenosis and aortic insufficiency.

H. H., aged thirty-one; male; single. Readmitted May 2, 1922, complaining of pain and limited motion in various joints, swelling and tenderness of interphalangeal joints, weakness, anorexia, and increasing dyspnea.

Family and past history essentially negative.

Present Illness.—Onset acute afebrile at the age of nineteen years, with sudden pains and stiffness of lower region of spine. During the four following months the condition became steadily worse and the entire spine became involved and rigid, forming a single large curve with convexity posteriorly. For four years afterward the condition of the spine gradually subsided with frequent periods of exacerbations of variable duration and severity, and then became completely arrested, until his second attack in 1922. Soon after the onset of the spondylitis patient also developed pain and limited motion in several other joints, especially the hips, but in these joints the arthritic symptoms rapidly subsided and never reappeared until the second attack in 1922. Soon after the onset of his disease the patient gradually developed moderate dyspnea on exertion, occasional palpitation of the heart, and occasional mild precordial distress, but at no time edema, coughing, or other cardiac symptoms. The cardiac symptoms subsided after a few months and reappeared in mild form only during exacerbations of his arthritis and in the beginning of his second attack. The course was always afebrile. Patient stopped working after the onset of his illness, but was up and about in the intervals between attacks. He resumed light work at the age of twenty-five and continued until his second attack in March, 1922. At this time he suddenly developed acute constant pains in the right lower chest, and two weeks later sudden pain and limited motion in various joints and swelling of the interphalangeal joints. With these arthritic symptoms he also developed increasing weakness, anorexia, increased dyspnea on mild exertion, but no fever and no other cardiac symptoms. Patient was readmitted to the wards with the above complaints.

Physical Examination.—Poorly nourished and developed adult male, of short stature, markedly stooped and kyphoscoliotic, moderately dyspneic on slight exertion, partially confined to bed. Head: Negative, except for poor condition of teeth, moderate hypertrophy of tonsils, and some tenderness in occipital region of head. Neck: All movements of head painful and markedly limited. Marked arterial pulsations and enlargement of cervical lymph-glands. Chest: Deep and pigeon-breasted in type. Respiratory excursion very small, breathing chiefly diaphragmatic. Heart: Moderately enlarged to left and to right. Apex-beat in fifth space 10.5 cm. to left of midline. Presystolic thrill over apex. Double mitral murmur with prolonged crescendo, presystolic murmur, and brief systolic murmur at apex. The first sound at apex as well as both second sounds at the base are accentuated. Faint systolic and early diastolic murmur at base. Arterial walls (brachial and radial) moderately thickened, but not sclerosed. Blood-pressure 110/30. Lungs: Marked emphysema; otherwise negative. Abdomen negative. Lymph-glands: Cervical, axillary, inguinal, and epitrochlear glands enlarged. Spine: Complete ankylosis of entire spine, forming a single large curve with the

convexity posteriorly. Small double scoliosis. Marked tenderness over lower dorsal and lumbar spine. Movements in several of the large joints of the extremities slightly limited and painful on extreme motion. Marked fusiform swellings of many interphalangeal joints, with tenderness and marked limitation of motion. Neurologic examination negative.

x-Ray of chest: Cardiac shadow slightly larger than normal. On account of slight torsion of cardiac shadow it is difficult to make accurate cardiac measurements.

Blood Wassermann and urinalysis negative.

Diagnosis: Chronic multiple arthritis of hypertrophic type; cardiac hypertrophy; chronic cardiac valvular disease; mitral stenosis and insufficiency; aortic insufficiency; pulmonary emphysema.

Course: Condition became again arrested in four months.

Both of the first 2 cases present definite valvular lesions, with hypertrophy and dilatation of the heart similar in every way to those which we are accustomed to see in chronic rheumatic heart disease. Arteriosclerosis, hypertension, and syphilis can be excluded as etiologic factors. In one of the cases there is no history of acute arthritis or antecedent infection which might be related to the cardiac condition; in the other one the disease commenced and progressed with acute infectious episodes.

An interesting feature of both these cases is the absence of symptoms of cardiac impairment in spite of the severity of the lesions. Indeed, neither of the patients was aware that he had a cardiac defect. We have found that it is the rule for the heart disease to pursue a symptomless course in these patients. This is due, undoubtedly, to the fact that the heart is rarely called on to meet the requirements of even moderate physical exertion, because of the enforced rest imposed on the patient by his joint disease. Thus, although the cardiac reserve power is impaired, the restricted mode of life of these patients makes no call on its depleted resources. We have noted too that in a number of patients with advanced valvular lesions the heart is only slightly or moderately enlarged. This probably depends on the same factor—the absence of the need for much compensatory adjustment.

The following case is presented to show how difficult it is at times to determine whether or not there is an organic heart lesion:

Case III.—Arthritis deformans; subacute onset; probable organic heart lesion.

S. G., aged sixteen; female, single. Admitted October 18, 1922, complaining of pains, swelling, deformities, and limited motion in almost all joints of the extremities, and inability to walk.

Family history negative.

Past History.—Infancy normal. Measles and diphtheria without complications in early childhood. Tonsillectomy for hypertrophied tonsils at seven years. Otherwise negative.

Present Illness.—Onset subacute at the age of nine and a half years, with occasional transient pains in both ankles, gradually becoming constant and severe, with swelling and tenderness, so that two months later patient became unable to walk. Gradually, at intervals of weeks, other joints of the extremities became similarly involved in the following order: knees, hips, shoulders, hands, and elbows, the involved joints gradually becoming painful, swollen, tender, deformed, with motion limited from slight at shoulders to complete ankylosis at wrists and hips. Several months after involvement of all joints her arthritis began to regress and patient again began to walk and use her limbs, though with marked limitation; but each winter of the following years there was a rather acute relapse of the polyarthritis, with mild fever, the condition lasting several months, then gradually regressing, but leaving her increasingly disabled. Chair- and bed-ridden for the last two years. Possibly mild fever during her first attack of arthritis, but none for twenty-three months after onset.

Physical Examination.—Poorly nourished and developed young female, chair- and bed-ridden. Head negative. Chest: Heart not enlarged. Apex-beat diffuse in fifth left interspace, $6\frac{1}{2}$ cm. from midsternal line. Action accelerated (96 per minute), regular, first sound at apex accentuated. P_2 accentuated. Systolic murmur at apex transmitted to axilla and back. Blood-pressure from 110/65 to 90/54. Lungs negative. Abdomen: Right kidney palpable, otherwise negative. Cervical, axillary, inguinal, and epitrochlear glands enlarged. Extremities: All joints of extremities involved with motion varying from complete ankylosis (wrists, hips) to only a slight limitation at both shoulder-joints. Marked hard periarticular swelling with deformities of some joints and varying tenderness of joints. Reflexes normal. No sensory disturbances.

x-Ray of joints shows advanced arthritic changes of the affected joints of the hypertrophic type.

x-Ray of heart: Heart approximately normal in size and shape, but there is some fulness in region of pulmonary artery (mitralization).

Cardiac dimensions: M. R., 3.2; M. L., 6.4.

Laboratory data: Urine negative; blood Wassermann negative.

Here is a case of deforming arthritis of seven years' duration, clearly on an infectious basis. The heart is not enlarged to physical examination, but on auscultation an apical systolic murmur transmitted to the axilla and to the back is heard. The

Roentgen plate suggests slight cardiac enlargement, and a slight prominence in the region of the conus arteriosus and pulmonary artery points to a mitral lesion. We believe that this girl has a mitral insufficiency, but realize that a positive diagnosis cannot be made at the present time.

Case IV.—Arthritis deformans; insidious onset; arteriosclerotic heart disease.

C. S., aged fifty-nine; male, married. Admitted December 11, 1922, complaining of pain and painful limited motion in many joints, difficulty in walking, and deformities, especially in hands.

Family history negative.

Past History.—Gonorrheal infection at eighteen, rapidly cured. At the age of fifty-two operation for inguinal hernia; otherwise essentially negative.

Present Illness.—Onset insidious at the age of forty-two, when patient began to have occasional pains and stiffness in various joints, especially in hands and feet. These pains became more frequent and prolonged, and several years later deformities of both hands and feet began to appear. For a number of years the arthritic condition appeared stationary and even improving until the age of fifty-two, when patient was operated on for inguinal hernia. While in bed a few days after the operation both knees became markedly involved and patient had to remain in bed four to five weeks, when the condition of the knee-joints improved. During the following years the arthritic condition gradually involved all joints of the extremities and part of the spine, the course being progressive, afebrile, with periods of exacerbations and remissions. No cardiac symptoms.

Physical Examination.—Well-nourished and developed elderly male, of medium stature, walking with great difficulty with the aid of a cane or crutches. Head negative except for poor condition of teeth. Chest: Fairly developed and symmetric. Respiratory excursions small and equal. Heart: Slightly enlarged to the left and downward. Apex-beat is moderately diffuse and weak, best felt in fifth space, 10 cm. from midsternum. Left border 11 cm. in same space. Action regular, rate 84. A loud rough blowing systolic murmur is heard best at the apex and transmitted around to the left axilla, A_2 stronger than P_2 . None accentuated. No murmurs at base. Blood-pressure 142/74. Moderate arteriosclerosis of peripheral vessels. Lungs and abdomen essentially negative. Orthopedic status: Advanced arthritic changes of hypertrophic type (confirmed by x-ray), involving all joints of extremities, also spine and temporomandibular joints. Marked bony periarticular swellings. Marked deformities, especially in hands. Neurologic examination negative. Blood Wassermann, blood chemistry, and urine examinations negative.

Diagnosis: Chronic multiple arthritis of hypertrophic type, general arteriosclerosis, chronic arteriosclerotic valvular disease, mitral insufficiency.

This case is presented in contrast to the others. The cardiac lesion can be explained on the basis of arteriosclerosis and moder-

ate hypertension. It is unnecessary to predicate an infectious etiology. Such cases are quite frequent in older individuals with chronic multiple arthritis, and must be clearly differentiated from those in the younger age groups with definite cardiopathies for which an infectious agent appears to be responsible.

Is this association of heart disease and arthritis deformans sufficiently common to be of significance? To answer this question we have, through the courtesy of Dr. P. W. Nathan, personally examined 80 patients with deforming arthritis on the orthopedic service of Montefiore Hospital. We have classed as positive infectious cardiac cases only those in whom arteriosclerosis, hypertension, and other etiologic agents could be definitely excluded. All cases in which there was some doubt as to the existence of an organic lesion of the heart, for instance, patients with murmurs and no enlargement, have been classed as doubtful as far as the heart is concerned. The diagnosis of heart disease on an infectious basis was made only in the presence of a diastolic murmur, either aortic or mitral, or a systolic apical murmur with cardiac enlargement in the absence of other possible causes for mitral insufficiency. The younger the patient, the more probable that our etiologic diagnosis is correct. In older individuals arteriosclerosis, hypertension, and occasionally syphilis often complicate the clinical picture.

Our cases, therefore, group themselves into four categories: (1) Infectious valvular disease. (2) Doubtful valvular disease. (3) Arteriosclerotic heart disease and heart disease associated with hypertension. (4) Normal hearts.

A review of the literature does not yield information of much value because of the fact that none of the observers have attempted to distinguish arteriosclerotic from inflammatory valvular lesions; and in many instances have accepted a systolic murmur alone as evidence of heart disease. The following table gives some of the published figures of the frequency of heart disease in arthritis deformans:

	No. of cases.	Per cent. with heart disease.
Charcot.....	41	5
McCrae.....	500	8
Blanc.....	200	7
Barjon.....	62	21
Bannantyne.....	293	17.9
Kast.....	24	25

An analysis of our series of 80 cases is presented in the following tables:

TABLE 1
PATIENTS WITH CHRONIC MULTIPLE ARTHRITIS

	No.	Per cent.	Average duration		
			Average age in years: of arthritis		Average duration
			At onset.	At present.	(years).
Infectious valvular disease...	14	17.5	28	38.4	10.4
Doubtful.....	11	13.75	30.1	38	7.9
Arteriosclerotic cardiopathies	22	27.5	54.4	64.1	9.7
Normal hearts.....	33	41.25	32.8	41.3	8.5
Total.....	80	100.00	37.5	46.5	9.1

TABLE 2

CLASSIFICATION ACCORDING TO AGE

	No. of cases.	Infectious valvulitis:		Doubtful:		Arteriosclerotic:		Normal:	
		No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
<i>Age at onset:</i>									
40 and under....	50	14	28	10	20	2	4	24	48
Over 40.....	30	0	0	1	3.3	19	63.3	10	33.3
<i>Present age:</i>									
40 and under....	33	9	27.3	6	18.2	0	0	18	54.5
Over 40.....	47	5	10.6	5	10.6	21	44.7	16	34

TABLE 3

CLASSIFICATION OF CASES OF INFECTIOUS VALVULAR DISEASE

Lesion.	No.
Aortic insufficiency.....	1
Mitral insufficiency with cardiac hypertrophy.....	3
Mitral stenosis and insufficiency.....	3
Aortic and mitral insufficiency.....	3
Aortic insufficiency with mitral stenosis and insufficiency..	1
Pericarditis with mitral insufficiency.....	3
Total.....	14

TABLE 4
CLASSIFICATION ACCORDING TO TYPE OF ONSET

Type of onset.	No. of cases.	Average age at onset (years).	Average age present	Infectious valvulitis:		Doubtful:		Arteriosclerotic:		Normal:	
				No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Acute.....	38	33	40.9	9	23.7	6	15.8	5	13.2	18	47.4
Subacute.....	15	38.1	45	2	13.3	4	26.7	4	26.7	5	33.3
Insidious.....	27	43.5	55.5	3	11.1	1	3.7	12	44.4	11	40.7

TABLE 5
CLASSIFICATION ACCORDING TO NATURE OF JOINT DISEASE

Joint lesion.	No. of cases.	Average age at onset (years).	Infectious valvulitis:		Doubtful:		Arteriosclerotic:		Normal:	
			No.	Per cent.	No.	Per cent.	No.	Per cent.	No.	Per cent.
Hypertrophic.....	54	38.8	11	20.4	5	9.3	15	27.8	23	42.6
Atrophic.....	26	35.5	3	11.5	6	23.1	6	23.1	11	42.3

The tables exhibit very graphically the great frequency of cardiac affection in chronic multiple arthritis, as well as the two types of lesions that must be distinguished. Clear-cut infectious valvular disease is found in 17.5 per cent. of all the cases, and in 28 per cent. of those in whom the disease started under the age of forty, and in no individual who was over forty at the commencement of his illness. Arteriosclerotic heart disease and cardiac hypertrophy following hypertension occur in 27.5 per cent. of all cases and in 66.6 per cent. of those who were over forty at the onset of their illness. Are we to deduce from this that under the category of chronic multiple arthritis we have really included two different types of disease of different etiology, or that the heart at different ages reacts in a different manner to the same noxious agent?

In view of the fact that, as is shown in Tables II and IV, the incidence of the different types of heart disease, as well as of several of the above-mentioned factors, is correlated so closely with the age of the patients, it becomes necessary to compare cases belonging to the same age groups. A study of the figures with this reservation does not allow of the conclusion that an acute or subacute onset, or course, or a hypertrophic type of lesions stands in a causal relationship to infectious valvular disease. The fact is rather that all of these manifestations are more common in the younger age groups and will therefore often be found in the same patient. Conversely, since an acute or subacute onset or course is less frequent in older individuals, it will occur less often in patients with arteriosclerotic valvular disease. The incidence of cardiac involvement in the two sexes is about equal. It is a well-known clinical observation that the heart valves are more prone to infection in younger individuals. This is shown clearly in the age incidence of rheumatic heart disease. We believe that, broadly speaking, the cases in our series are of the same nature, and that the greater incidence of infectious valvular disease in the younger age groups is due to the greater vulnerability to infection of these hearts.

The use of the term "infectious valvular disease" requires a word of justification. We have ventured to ascribe an infec-

tious etiology to these lesions because of their great similarity to those valvular defects which are known to be induced by an infectious agent. We are at a loss to explain them on another basis. If this interpretation is correct it gives added evidence for the infectious nature of many cases of chronic multiple arthritis.

The frequency of arteriosclerotic heart disease and cardiac enlargement in the older age groups is greater than one would expect to find in a control series; 27.5 per cent. of all the cases and 66.6 per cent. of those who were over forty when the arthritis began give evidence of this type of cardiopathy. The average age of these patients is 54.4 years. We have placed in this category patients who had enlarged hearts with apical or basal systolic murmurs, with signs of peripheral arteriosclerosis, or with hypertension. The evidence is presumptive that the heart lesion is due to sclerosis of the mitral or aortic valve, or secondary to hypertension. It is true that some of these cases may have had infectious valvular disease, but the uncertainty of that diagnosis is so great in older individuals in the presence of arteriosclerosis and hypertension that we have deliberately excluded them from this category. Other authors have called attention to the frequency of arteriosclerosis of the aorta and aortic valve in patients with arthritis deformans.

It would lead too far afield to prolong this discussion. We have presented these 4 cases, and an analysis of a series of 80 cases of arthritis deformans, in order to emphasize the frequency of cardiac involvement in chronic multiple arthritis and to demonstrate the main types of lesions, the infectious valvular disease, the arteriosclerotic valvular disease, and the cardiac hypertrophy secondary to hypertension.

CLINIC OF DR. MAY G. WILSON

NEW YORK NURSERY AND CHILD'S HOSPITAL

THE CLINICAL VALUE OF VITAL CAPACITY AND EXERCISE TESTS IN THE MANAGEMENT OF CHILDREN WITH ORGANIC HEART DISEASE*

In children with heart disease a knowledge of the capacity for physical activity is of the utmost practical importance. The determination of the advent of cardiac failure, the stage of convalescence, the day of return to school, the ability to climb stairs, as well as the choice of out-door games, are some of the practical questions the physician must consider. Such information is not always available from the history and physical examination alone. This is particularly true when dealing, on the one hand, with the overanxious or non-observant mother, and, on the other hand, with the timid or fearless child.

Recent investigations have indicated the need and value of establishing some clinical standards of circulatory function or efficiency, while at the same time emphasizing the difficulty of obtaining any exact estimate of the cardiac reserve. The two most accepted clinical methods are any standardized test exercise and the vital capacity. We have in previous communications,^{1, 2} on Exercise Tolerance of Children with Heart Disease described standardized test exercises and standards for normal vital capacity. The clinical value of these tests in the case of children with heart disease is the subject of today's clinic.

The practical application of these tests is best demonstrated in the use of the functional classification of organic heart disease adopted by the Association for the Prevention and Relief of

* From the Department of Pediatrics, Cornell University Medical College, and the Cardiac Clinic of the New York Nursery and Child's Hospital. This study has been aided by the F. K. Sturgis Fund for Cardiac Research.

Heart Disease in use in most cardiac clinics. In the Cardiac Clinic of the New York Nursery and Child's Hospital this classification has been amplified as follows:

Class 1. Organic. (Able to carry on habitual activity):

As determined by careful history and physical examination.

As controlled by vital capacity test. (A vital capacity within normal limits.)

As checked by an exercise test: Able to tolerate an average or severe test exercise, *i. e.*, Staircase test, four flight rise of 30 feet in twenty to forty seconds. Dumb-bell test: Swing two 4, 5, or 7 pound dumb-bells twenty to thirty times, two seconds for each swing.

May be permitted to attend school, take part in all but competitive school athletics.

Out-door sports may include walking, skating, cycling, baseball, tennis. (All exercise to be carried on well within the limits of fatigue.)

Class 2, A. Organic. (Able to carry on slightly diminished physical activity):

As determined by physical examination and history of symptoms following usual activity.

As controlled by vital capacity test: Reduction of vital capacity of 10 to 25 per cent., other factors known to diminish the vital capacity being excluded.

As checked by an exercise test: Unable to tolerate an average or severe test exercise, but able to tolerate a mild test exercise, *i. e.*, staircase test, two flight rise of 15 feet in forty seconds. Dumb-bell test: Swing two 4, 5, or 7 pound dumb-bells ten to fifteen times, two seconds for each swing.

May be permitted to attend school under supervision and take part in restricted exercises. This can best be done at a Convalescent Home.

Indulge in graduated exercises and physiotherapy.

(Should report weekly for observation.)

Class 2, B. Organic. (Able to carry on greatly diminished physical activity):

As determined by physical examination and history of symptoms following habitual activity.

As controlled by vital capacity test: Reduction of vital capacity of 25 to 40 per cent., other factors known to diminish the vital capacity being considered.

As checked by an exercise test. Unable to tolerate the mild test exercise, but able to tolerate only slight exercise, *i. e.*, one flight of stairs in forty seconds.

Should not be permitted to attend school.

Is best taken care of in a Convalescent Home.

May have physiotherapy and graduated exercise.

Should have daily periods of rest and be under close observation.

Class 3. Organic. (Unequal to any physical activity):

As determined by physical examination and history.

As confirmed by vital capacity: Reduction of vital capacity of 40 to 80 per cent.

Unable to tolerate any exercise, having symptoms at rest.
Must have absolute rest in bed.

This amplified classification has proved of great value in indicating to nurses, clinics, convalescent homes, social workers, and the schools the status of the case from the only standpoint in which they are interested, namely, what may the child be permitted to do. It is very important to keep in mind, however, that any classification holds for a variable length of time and is dependent upon possible further developments. As a rule, a Class I case will retain its classification until the occurrence of some further infection. It is our routine to impress the fact that after any intercurrent illness the child must return for re-classification. Cases classified 2, A or 2, B may be convalescent from a Class 3 or going on to a Class 3. In either case the child should be seen at least weekly and be observed closely, the occurrence of any clinical symptoms taking precedence over classification.

For a detailed description of method and technic of vital capacity and exercise tests used the reader is referred to the communications previously referred to. The vital capacity test is simple and practical. A spirometer is part of the equipment of most cardiac clinics. The vital capacity is taken routinely by an assistant at each visit, the entire process occupying about five minutes for each case. The use of a special chart (Fig. 41) enables a reading in percentage of normal to be recorded without any calculations.

The child is comfortably seated in front of the spirometer with body erect and shoulders back. The tube leading to the spirometer with a clean mouth-piece attached, is then held in the hand and the following steps are carried out successively and with due care:

- (1) The deepest possible inspiration (breath) is taken.
- (2) The mouth-piece is quickly placed into the mouth and held tightly between the lips.
- (3) The breath is rapidly and completely blown into the spirometer (empty feeling).
- (4) The reading of the instrument is taken and a record made of it.

The highest number of cubic centimeters recorded in from three to five satisfactory trials is accepted as the vital capacity. An interim of about one minute should usually be given between repeated tests.

Chart I, A

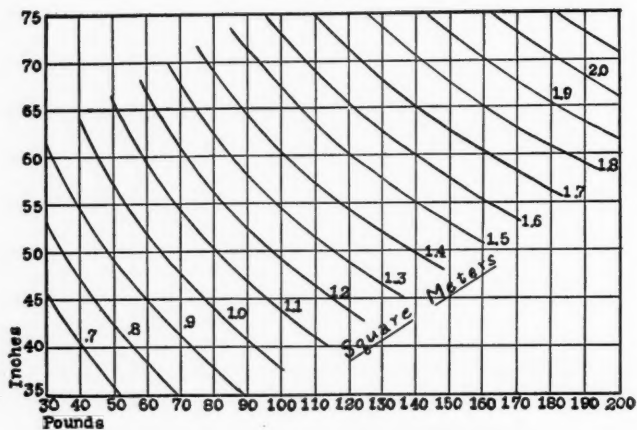


Chart for deriving body surface area from height
(in inches) and weight (in pounds). Modified
from BuBois chart, Arch. Int. Med. 17, 863.

Fig. 41.—The technic of vital capacity measurements on children.

Chart I, B

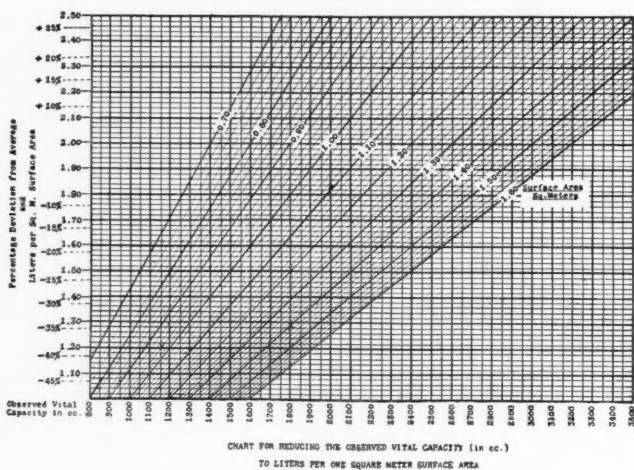


CHART FOR REDUCING THE OBSERVED VITAL CAPACITY (in cc.)
 TO LITERS PER ONE SQUARE METER SURFACE AREA

Fig. 42.

Certain precautions must be observed. Only one inspiration should be taken and this should be the fullest and deepest inspiration; it should also be completely expelled. Children are likely to try too hard and fix the chest, holding the breath so that only the air in the upper passages is expelled. Or they are apt to remove the mouth-piece before the chest is completely emptied. If one is on the lookout these difficulties may be overcome with a little coaching.

Directions for Using Graphic Charts

I

A. B.

- (1) Obtain net weight in pounds and net height in inches.
- (2) Find surface area in square meters on Chart I, A.
(e. g.) John: Weight 55 pounds. Height 50 inches. . . . Surface area 0.94 square meters.
- (3) Determine vital capacity measurement in cubic centimeters.
- (4) Find on Chart I, B the point of intersection of the vertical line (of the observed vital capacity in cubic centimeters) with the oblique line (of the calculated surface area in square miles). Then transpose this point of intersection to the left margin by following along the nearest horizontal line, and read the vital capacity in liters per square meter and the percentage of the normal.
(e. g.) John: Surface area, 0.94 square miles; vital capacity, 1650 c.c.; liters per square mile surface area, 1.76—; 10 per cent. below average normal.

The test exercises used (Fig. 43) are the staircase and dumb-bell tests. The parent or another child may assist in recording the numbers, the entire process occupying about five minutes for each case. The staircase test is particularly useful for timid children and if the parents are apprehensive. Should the child be unaccustomed to physical exercise and the arm muscles poorly developed, the dumb-bell test should be substituted by the staircase test. As a rule boys enjoy the dumb-bells.

A test exercise is considered to be tolerated if satisfactorily performed, and when on completion there is no apparent general exhaustion, although the arms may be tired. The color of the face is flushed, the respirations are increased slightly in depth and frequency, the systolic blood-pressure shows a normal curve, i. e., a rise of 10 to 40 mm., with maximum readings within twenty to forty seconds, and a return to normal within two minutes (Fig. 44). This is the reaction obtained with average normal children to these test exercises. Any other test exercise that makes a definite demand on the physical capacity may be substituted, provided the reactions of a sufficient number of

STANDARDIZED TEST EXERCISES

Test Exercises	Age in Years for Standard Weight and Height	Normal Range															
		Simple or Mild			Average				Severe or Strenuous								
		No. of D.B.	Weight, Lbs.	Swings, Times	No. of D.B.	Weight, Lbs.	Swings, Times	No. of D.B.	Weight, Lbs.	Swings, Times	No. of D.B.	Weight, Lbs.	Swings, Times				
Dumb-Bell Test:																	
Swinging two iron dumb-bells from the floor to full stretch of arms overhead and back again between the legs at a constant rate of two seconds for each swing	6-8	2	3	10	2	3	20	2	3	30	2	3	30				
		2	4	10	2	4	20	2	4	30	2	4	30				
	8-12	2	4	10	2	4	20	2	4	30	2	4	30				
		2	5	10	2	5	20	2	5	30	2	5	30				
	12-15	2	5	10	2	5	20	2	5	30	2	5	30				
		2	7	10	2	7	20	2	7	30	2	7	30				
		2	10	10	2	10	20	2	10	30	2	10	30				
		2	10	10	2	10	20	2	10	30	2	10	30				
		2	10	10	2	10	20	2	10	30	2	10	30				
		2	10	10	2	10	20	2	10	30	2	10	30				
	Staircase Test:																
	Stairs taken at a steady climb without rest.....	6-14	2	15	40	4	30	40	4	30	20						
Reaction of Average Normal Children Following Test Exercises																	
		To the Mild Test Exercise			To the Average Test Exercise			To the Severe Test Exercise									
Color of face (flushed).....					+			++									
Degree of dyspnea.....					+			++									
Degree of fatigue.....								+									
Rise of systolic blood pressure.....		10-15 mm.			20-30 mm.			30-40 mm.									
Type of systolic curve.....		Normal			Normal			Normal									

Fig. 43.

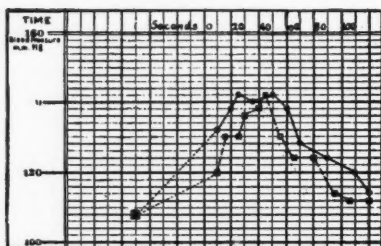


Fig. 44.

normal children are first studied and standardized for comparison. It is essential to be familiar with the general and circulatory reactions of normal children to these test exercises to

intelligently interpret the reaction of children with heart disease. It is also important to inquire as to the previous exercise tolerated, as a child unduly restricted or a convalescent cannot be expected to have a maximum normal tolerance, such as is obtained in a child who has not been restricted and has indulged in strenuous exercises. Children with a wide normal range of systolic blood-pressure, or those having a high blood-pressure give bizarre systolic curves that are difficult to interpret. This is particularly observed in the unstable, nervous child. However, in our experience, these cases have been in the minority. Many of the children have been tested over a period of years and have shown remarkably constant reactions. There need be no fear in giving a child with heart disease a test exercise. We have only observed one case in which there was an apparent collapse, attributed at the time to the test exercise. She, however, had a similar collapse on being told to enter the hospital. It was also learned that, in order to have her way at home, she would with very little effort suddenly tremble, grow pale, perspire, and faint. However, a test exercise should never be given to a Class 3 case or to a case with a recent carditis for at least two weeks after a normal temperature. If a diminished tolerance is expected, a mild test exercise should be always the first one given.

A test exercise is considered not to be tolerated if during the exercise or at the completion there is undue exhaustion or delayed recovery. The respirations are rapid, shallow, and labored. The face is pale and there may be profuse perspiration. The systolic blood-pressure curve is abnormal, *i. e.*, an initial fall, or a slow rise of 20 to 60 mm. with maximum readings delayed or prolonged fifty to one hundred and twenty seconds or more, with a return to normal delayed three to six minutes. This is the reaction to a test exercise which is tolerated by normal children, and it is similar to the reaction obtained in normal children who have been given a greater amount of exercise than they have been able to tolerate (Fig. 45). The degree of the general and circulatory reactions to the particular test exercise classifies the case as 2, A or 2, B. In analyzing the

systolic blood-pressure curve it is essential to consider the fall or rise, amount of rise, and return to normal, as well as the time of maximum readings, before designating the curve as normal or not. Frequently a delayed return to normal will be the first indication of an abnormal curve; a slight increase in work will bring out a delayed rise or prolonged summit. The blood-pressure curve is an excellent check on personal observation of the general reaction. A record of the reaction to a previous test exercise is of great value for comparison. As a general rule, we do not follow the pulse after exercise, as it requires a trained assistant, who is not always available.

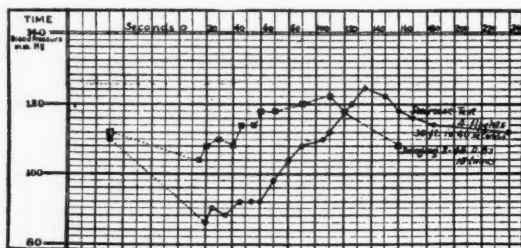


Fig. 45.

In a previous paper we have shown that the vital capacity measurement may be accepted as a substitute for an exercise test, provided all other factors known to diminish the vital capacity have been excluded. The vital capacity test may be used for all types of cases, and particularly adapted for bed cases (Class 3). As a rule the vital capacity within normal limits indicates a normal exercise tolerance, and a test exercise may be omitted. A reduction in vital capacity of 10 per cent. or more must be checked by an exercise test because of the possibility of the presence of other factors which may diminish the vital capacity. Once a normal vital capacity has been recorded, subsequent readings will be found to closely follow and indicate the clinical course. Here, as with exercise tests, due consideration must be given the expected normal range for the individual case, since a child accustomed to strenuous exercise

may be expected to have a higher normal than one who has been restricted, and slight reductions have more or less significance. Daily vital capacity readings are useful in following up the therapeutic action of digitalis.

A diminished exercise tolerance, as indicated either by a gradual increasing reduction in vital capacity or a diminishing tolerance for test exercise, has been observed in many cases to precede the advent of the definite signs of cardiac failure by from two to six weeks. It is, as a rule, not associated with definite complaints from the child, but may be associated with some loss of weight, increase of pulse-rate, and a slight temperature.

The use of the exercise test and vital capacity as an index of the tolerance to other forms of exercise has been to some degree empiric. A practical demonstration of the validity of this assumption has been the close agreement that has obtained between the clinic classification and the ensuing course of the case. For the past four years 125 children have been classified in the clinic and segregated in special cardiac classes in the public schools of New York City. These children have been observed daily from 9 to 5. Their activities indoors and out have been closely observed and recorded; these school reports, including weight, temperature, and pulse readings, have been filed in the clinic. With this close follow-up we have been able to judge of the correctness of our classification. The consensus of opinion of the nurse and teachers was that the children held close to their classification.

It is important to remember that the greater number of children with organic heart disease are of Class 1. It has been estimated recently⁵ that 0.7 per cent. of every 100 school children in New York City have organic heart disease. Of that number 55 per cent. are Class 1; 37 per cent. Class 2, A; 7 per cent. Class 2, B, and 1 per cent. Class 3. The census of our clinic today shows that of 140 organic cases, 75 per cent. are Class 1; 16 per cent. are Class 2, A; 5 per cent. are Class 2, B, and 3 per cent. are Class 3. A comparison of the distribution of cases classified by clinical examination alone with that of those

indicating the physical capacity of children with organic heart disease. A careful history and physical examination supplemented by these tests would seem to be the best practical method at present available for the classification and management of children with heart disease. The following cases will illustrate the practical and clinical value of these tests:

Case I.—E. G. first came to the Cardiac Clinic January, 1920, at twelve years of age. The past history was as follows: Occasional sore throats, frequent growing and joint pains, and a mild arthritis. Cardiac involvement was of four years' duration. Tonsillectomy was refused. She was excused from school athletics and was restricted from free play, but admitted to taking part in all games equally well with her schoolmates. The clinic history from January, 1920 to January, 1924 is as follows: Except for an occasional sore throat and some joint pains and a mild rheumatic fever in April, 1922, she has been very well, the diagnosis being throughout this time mitral lesion, Class 1. She has developed into a splendid girl in good physical condition. Graph of Case Record I is a true objective picture of her physical capacity and confirms the clinical history for the past four years.

Comment.—The persistent reduction of vital capacity of 10 to 13 per cent., notwithstanding a normal exercise tolerance for the severe test exercise, may be explained by the radiographic evidence of increased hilum shadow and thickened lung markings radiating to the periphery. These x-ray findings are, as a rule, associated with a reduction in vital capacity of 10 to 20 per cent. The gradual increase in vital capacity from 1900 to 2100 c.c. during four years is in accord with increased growth and development. It is of interest to note that the same percentage reduction from normal is still present.

Case II.—A. W., boy, ten and a half years of age, first came to the Cardiac Clinic in November, 1920, and has been under our care for the past four years. The past history consists of a mild sore throat and a severe chorea at five years of age, followed by cardiac involvement. The boy attended regular school and stated that he climbed five flights of stairs to his home equally well with his brothers. Physical examination showed a boy of poor nutrition and development, with enlarged tonsils and a mitral lesion. The vital capacity was minus 6 per cent. and he tolerated an average test exercise. He was classified as a Class 1. Subsequent history: The boy was admitted to a special segregated cardiac class. The accompanying graph of Case Record II shows that after four months his vital capacity increased to normal limits, and tonsillectomy was performed, with an uneventful recovery. In July,

1921 he went to a regular boys' camp which his brothers attended. While there he hiked, went swimming, and did not restrict his activities. He reported to the class September 15th in apparent excellent physical condition, stating that he felt perfectly well. Vital capacity record, however, showed a reduction in vital capacity, and he was advised to return to the special class for daily observation. October 15th he returned to the clinic for examination. He admitted some joint pains, and the school reported a change in disposition and a tendency to nervousness. The vital capacity showed a still further reduction. The boy was ordered to bed much against his wishes and returned to the clinic November 1st refusing to remain at home. The vital capacity showed a slight increase and he was allowed to return to school on a cot. The daily school record from November 1st to November 28th showed a pulse ranging from 85 to 100, temperature of 99° F., and some loss of weight. During these four weeks the boy rebelled against remaining on a cot and being carried upstairs to his home. The increasing reduction of his vital capacity was a true index of his clinical condition and prognosticated the acute carditis which ensued. He was admitted to the hospital ward on November 29th, with a diagnosis of acute carditis, aortic insufficiency, mitral stenosis, Class 3. While at the hospital daily vital capacity records showed a rapid increase in vital capacity for fourteen days, which was coincident with clinical improvement, and the boy was taken home against advice, only to return in a week. His further progress was slow, and he was permitted to return to school on a cot when attaining a classification of 2, B. He refused to remain at home in bed. Eight months after his carditis he attained a classification of 2, A, and returned to camp in July, 1922, under restricted exercise. While there he gradually tolerated all but strenuous hikes and swimming. He returned to the clinic in September, 1922. At that time his vital capacity had reached normal limits and he was classified as a Class 1, and has retained this classification for the past two years.

Comment.—This case illustrates well the value of some objective test to determine physical capacity. This boy would never admit his incapacity, and were it not for the confirmative evidence afforded by these tests I do not believe we could have convinced his mother. The diminished vital capacity was important confirmatory evidence of the oncoming carditis and preceded the earliest clinical symptoms.

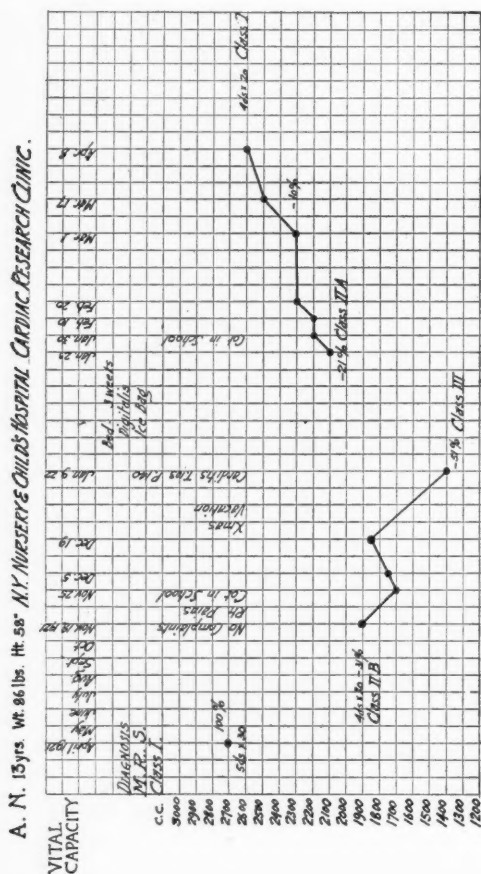
Case III.—C. V., girl, nine years of age, was first seen at the Cardiac Clinic on January 16, 1922. Her only complaints were loss of appetite and general malaise. The mother thought the child was well and tolerated exercise equally well with playmates. The past history revealed occasional sore throats, transient arthritis, and severe joint pains of three days' duration at six years of age. She was never known to have heart trouble. Physical examination showed a pale girl, underdeveloped, tonsils small and cryptic, lungs clear, D'Espine to the second dorsal, heart not enlarged, with a soft

a vital capacity of minus 24 per cent. classified the case as 2, B, and the child was allowed out of bed. A month later she was permitted to attend school on a cot until a vacancy was available in a Convalescent Home. On June 16, three weeks later, the vital capacity was minus 18 per cent. In order to determine if this reduction in vital capacity was a true index of the exercise tolerance, an exercise test was given. She was unable to tolerate an average test exercise. After a month's stay at the Convalescent Home she returned to the clinic, and was found to have a vital capacity within normal limits and was able to tolerate an average test exercise. She was classified as Class 1, and retained this classification for seven months. In February, 1923, after an acute respiratory infection, she began to show some loss of weight. On March 16th her vital capacity showed a reduction and she was put in Class 2, A. A week later (April 18th) she developed a high temperature and a recurrent acute carditis with nodules. May 7th, following a week of normal temperature, the vital capacity showed an increase to 1800 c.c., a more rapid recovery than in her initial attack. After a tonsillectomy in June and a stay in a Convalescent Home she returned in the fall in splendid general condition, showing a vital capacity of 2100 c.c.

Comment.—This case again illustrates the value of functional tests in warning of the advent of a carditis before the clinical symptoms are sufficiently clear. This case also illustrates that the vital capacity may be used a factor in determining when a child may be permitted out of bed. This case also indicates every attack of carditis is not of equal severity or may not require the same period of convalescence.

Case IV.—See graph of Case Record IV. A. N., well-developed boy, thirteen years of age, was referred to the Cardiac School April 21, 1921. He stated that he was perfectly well and able to compete with his schoolfellows and refused to enter the special class. His past history was as follows: Tonsillectomy at six years of age, a chorea at ten years of age, and frequent growing and joint pains for the past year. His mitral lesion was found accidentally at nine years of age by a school physician. His vital capacity was 100 per cent., and he tolerated a severe test exercise. The diagnosis was mitral stenosis, Class 1. On November 11, 1921 he was sent for by the school nurse for follow-up. He did not wish to come to the clinic, stating that he was very well. On examination he did not disclose anything of moment, but the vital capacity showed a reduction of 31 per cent. and he could not tolerate a severe test exercise, but was able to tolerate an average test exercise. Because of these findings he was induced to enter the special class and was put on a cot for observation. On November 25th he was admitted to school and remained there until December 19th, when he returned home for Christmas vacation. During the time at home he had some rheumatic pains, was not up to par, but refused to go to bed. On examination January 4, 1922 the boy

was found to be pale, slightly dyspneic, the vital capacity showing a reduction of 51 per cent. He was classified as Class 3 and ordered to bed. Four days later he was seen at home acutely ill with a definite pericarditis. On January 23d he was brought for examination to ascertain whether he could be per-



Comment.—This case illustrates very well the value of having a previous record of vital capacity and exercise test, for not knowing the boy we would not have noted the significance of a vital capacity of 1900 c.c., since the reduction from the average would only have been about 20 per cent. Likewise, the fact that he was able to tolerate an average test exercise would have passed him as a Class 1 were it not for the fact that a previous record showed him able to tolerate a severe test exercise. It is important to remember the upper and lower possible normal limits. This boy is a typical example of the type that overestimates his ability and never gives in. He also illustrates the possible speedy recovery from a severe carditis which would ordinarily have indicated at least six weeks' rest in bed (which was ordered, but refused, apparently with no ill effects). This case must have had very little permanent involvement of the cardiac muscle.

Case V.—H. C., girl, ten years of age, was brought to the Clinic September 23, 1921, complaining of cough, dyspnea, and swelling of ten days' duration. Her past history consisted of infrequent sore throats, chorea at four and six years of age, rheumatic fever at ten years of age. Cardiac involvement was not known. For the past week she has not felt well and has had some joint pains. Physical examination showed a girl acutely ill, with apparent good general nutrition. Some cyanosis and edema of the face, dyspneic, with respirations 40, and pulse 130. Throat was red, lungs congested, liver tender, heart enlarged, with a systolic and diastolic murmur. The vital capacity showed a reduction of 55 per cent., confirming the clinical diagnosis of cardiac failure. She was admitted to the ward and the accompanying graph of Case Record V indicates the clinical course. The daily increase of vital capacity was coincident with the rapid disappearance of symptoms. On October 12th tonsillectomy was performed, with an uneventful recovery, and the child was sent to a Convalescent Home. December 2d she attained a vital capacity of minus 26 per cent., which is the highest that she has ever reached. Except for a relapse in six months she has been very well up to the present time. She has never reached a Class 1 classification.

Comment.—This case illustrates the use of the vital capacity as a possible therapeutic guide in the administration of digitalis. She is also an example of the type of case that probably never reaches a normal vital capacity.

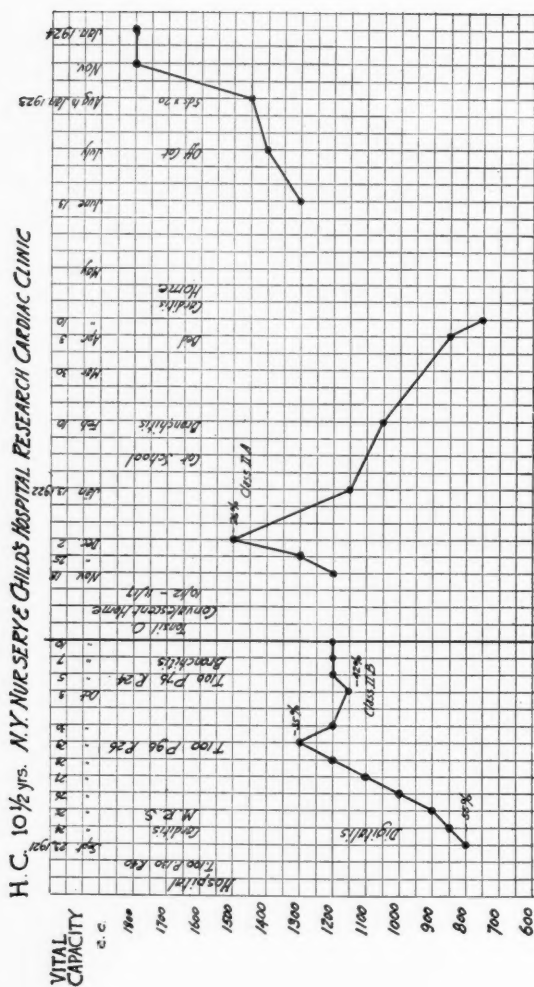


Fig. 50 (Case V).

Case VI.—M. M., girl, ten years of age, admitted to the ward February 4, 1921, with cough and high fever. Past history: Frequent recurrent attacks of bronchitis and sore throats with occasional joint pains. Cardiac condition was not known on admission. Physical examination revealed a well-developed girl acutely ill, with tonsils large and congested, lungs full of moist

râles, liver tender, no edema, heart enlarged, with a systolic and diastolic murmur. Temperature 104° F., pulse 118, respirations 32. Vital capacity minus 82 per cent. The accompanying graph of Case Record VI of the vital capacity shows a rapid increase of vital capacity to about 50 per cent. in twelve days. On March 2d, while still in the hospital in bed, a reinfection brought the vital capacity down to minus 60 per cent., with a return to previous level in two weeks, at which it remained for the ensuing two years.

Comment.—This case again illustrates the type of case that never becomes a Class 1. It is interesting to note that her best vital capacity is about minus 40 per cent. However, she was able to tolerate a mild test exercise, the increased reduction in vital capacity being due no doubt to the recurrent bronchitis.

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CLINIC OF DRS. HERBERT J. WIENER AND HENRY ELSNER MARKS

FROM THE DEPARTMENT OF METABOLISM, VANDERBILT CLINIC

THE TREATMENT OF DIABETES IN AMBULATORY PATIENTS

THE treatment of diabetes in office or clinic practice presents problems which are not encountered in the hospital treatment of this disease. The hospitalized patient is subject to a degree of control which compares with that of the physiologic laboratory, especially in the case of hospital services organized for metabolic research such as those from which much of the recent clinical investigation of diabetes has come. In private practice the patient is less well controlled, but here the close personal contact with the physician and the fact that the patient has sufficient means to make the special dietary routine easy facilitate the management of the case. Furthermore, when advice is paid for it is more willingly followed.

In the diabetic clinic, however, allowance must be made for the difference in the degree of control over the patient and in the type of patient with whom we have to deal. It is our purpose in this paper to discuss the management of these patients, with especial reference to the methods by which the recent developments in treatment may be applied to them. The special problems encountered may be summed up as follows:

1. Less direct control of diet and other therapeutic measures. Consequently the development of morale and self-control is a special and necessary part of the treatment of these patients.
2. Greater difficulty in the carrying out of diet and other forms of treatment owing to economic, domestic, and other circumstances in the patient's life. This means that the treatment prescribed in each case must be considered from the

point of view of the patient, and calls for a routine diet which is, above all else, simple and easily managed in any household, and yet sufficiently diversified to be kept up indefinitely.

3. Less frequent contact with the patient, necessitating a greater margin of safety in the diets used.

4. Less accurate quantitative estimation of diet, which must be met by the use of those foods which lend themselves most easily to quantitative measurement.

It is evident that the means employed for meeting these problems fall into two groups: those directed toward the treatment, to simplify it and make it less difficult for the patient to carry out, and those directed toward the patient, to educate him or, rather, to modify his mental attitude. In addition, the routine used must facilitate the work of the physician and reduce the amount of time and attention required by the individual to a reasonable degree. In other words, while the patient must be studied and treated individually, from a practical standpoint this is best accomplished by the use of a general routine applicable to most cases, but easily susceptible of modification to meet individual requirements.

In all diseases requiring prolonged and constant dietary restriction the patient's mental attitude toward his condition and his diet is likely to be the determining factor as regards success in treatment. In the case of these diabetics it is often the sole factor. The physician must realize this and direct his efforts accordingly toward inducing a favorable attitude in the patient, which means one of active co-operation and willing self-control. To this end he must study the patient's character and emotional reactions and, like the advertising man, direct his appeal toward the most susceptible spot. Most patients come to us with the question uppermost in their minds, "How much can I have to eat of the forbidden foods, and what can I do to get more of them?" Often a patient says, "I must have a certain amount of bread, I cannot live without it." Many feel that life is not worth while if they cannot make the satisfaction of appetite a source of pleasure. It is this attitude of mind that foreshadows the downward progress of the average

diabetic, and our success in changing it determines our success in treatment. The diabetic must ask himself not "How much can I have?" but "How can I live comfortably and satisfactorily on the foods that I am allowed?" If he exercises ingenuity in the compounding of the foods which he is permitted he can have a sufficiently varied and appetizing diet, and it is the realization of this that we must first inculcate in the patient. The physician can do much by a few simple suggestions as to the preparation of foods, the use of condiments, various methods of cooking, the preparation of vegetables with butter or with cheese, etc., and can suggest means which will help enormously in families where cooking is an unknown art. If the services of a visiting dietitian are available a practical demonstration of simple methods of food preparation can be of the greatest value.

Much can be done in a few minutes at the first visit by a concise explanation of the cause and nature of the disease, contrasting the prognosis in treated and untreated cases, and explaining the absolute dependence of prognosis on dietary control. The patient who understands these things clearly is well prepared for an experimental period of complete restriction. Too often he has been led by his family practitioner to believe that a decrease in urinary sugar is an indication of satisfactory treatment, and that if he can find an easy diet which will give him "only a little sugar" in the urine, the prognosis will be good. Experience shows that such half-way measures are not satisfactory, and the patient who is allowed to have a little sugar in the urine will much of the time have a great deal, and, most important of all, will have a lax attitude toward his treatment and a lack of self-discipline which will almost surely terminate in repeated indiscretions and progressive loss of tolerance, with the inevitable outcome.

The patient then is made to understand that he must submit to a week of rigid dietary restriction. As a matter of fact, the diet which he is given, as will be explained below, is almost always a maintenance diet, the expected hunger-pangs and weakness (which not infrequently he has had acquaintance

with under the starvation treatment) fail to materialize, and he is well pleased at finding that the week of most severe restriction has meant no real discomfort, especially if he also finds that it has made him sugar free, and that with little or no loss of weight. Such an outcome of the first week's treatment smoothes the way for all that follows. When it does not occur the failure is to be attributed to one of three circumstances—a severe grade of diabetes, unintentional error or imperfect understanding of the dietary directions, or a resistive patient with strong convictions about the impossibility of getting along without certain foods. In the first instance more stringent restriction or the use of insulin is indicated, in the others further explanation should set things right.

The importance of the maintenance diet is not always sufficiently appreciated. While it is obvious that a submaintenance diet cannot be continued indefinitely, nevertheless there has been a feeling that undernutrition is not only frequently unavoidable, but that it is of benefit rather than otherwise in most cases. This was largely due to the dictum that undernutrition has a favorable effect upon carbohydrate tolerance. It is true that in undernutrition the basal metabolic level and the total metabolism are lowered. Not only is the total energy requirement lessened through the diminished size of the patient, and especially the diminished mass of his active cellular tissue, but the rate per square meter (or per unit mass of active tissue) is decreased, a means of conserving the body's fuel resources. This effect manifests itself in the muscular weakness and fatigueability, the susceptibility to cold, the lowered body temperature, and bradycardia. At this lowered metabolic level, of course, the subcaloric diet may become a maintenance diet and energy equilibrium may be achieved in this manner. We are not, however, convinced from our material that there is an increase in carbohydrate tolerance at the same time, that is, in the total amount of carbohydrate which the body is able to metabolize.

The difficulty in overcoming glycosuria on a maintenance diet in the past was due partly to inadequate comprehension of the rôle of protein and largely to the fear of bringing on acido-

sis by high fat feeding, with the consequent feeling that the caloric requirement must be made up by the use of protein.

The work of Newburgh and Marsh, Woodyatt, Shaffer, and others has set at rest the fear of high fat feeding, and has shown that if protein is reduced to the minimum required for nitrogen equilibrium fat may be given in relatively large quantities without harm.

Protein is metabolized, except for the NH_2 groups and a small proportion of cyclic amino-acids, as glucose and fatty acid. The glucose yield of the common proteins is about 58 per cent., and this must be added to the carbohydrate taken as such in calculating the total carbohydrate of the diet; in addition, 10 per cent. of the neutral fats, representing the glycerol component, is capable of being metabolized as glucose, and should be included in the total carbohydrate. Thus the available carbohydrate of the diet is determined.

The question of how much fat may be given without ketone formation cannot be answered with certainty, for the theory of ketogenesis is still in many respects *sub judice*. It has been shown that the normal combustion of fat to CO_2 and H_2O requires the simultaneous combustion of carbohydrate; in the absence of the latter, beta-oxybutyric acid is formed, and this is further oxidized to the ketone bodies, diacetic acid and acetone. When these abnormal acids are present in the body in sufficient quantity to lower the alkali reserve appreciably acidosis is added to the diabetes. About 4 grams of fat may be burned, apparently, without ketone formation, for each gram of available carbohydrate, depending upon the molecular weight of the fat. This ratio, however, appears to be variable, and it is possible that protein metabolism has some bearing upon the question. At times reduction of the protein intake appears to have a favorable effect upon ketone formation out of proportion to the quantitative reduction in fatty acid intake which it implies, or to the favorable effect upon carbohydrate tolerance which may follow upon the reduction in total available carbohydrate.

The effect of fat feeding up to the caloric requirement of the body in sparing the destruction of tissue protein for energy must be kept in mind as an important factor. If the patient on a submaintenance diet has abundant fat stores his body protein is well protected and the first stages offer no difficulty. But if he is already poorly nourished and is excreting sugar it will be difficult to overcome the glycosuria by starvation or undernutrition. Let us suppose that a patient whose maintenance requirement is about 1600 calories is put upon a starvation period. In an extreme case without available fat this must be supplied by body protein, which will be consumed at the rate of about 400 grams daily. The available carbohydrate (58 per cent.) from this will amount to about 232 grams. It is difficult to understand how one could hope to clear up the glycosuria more quickly by a starvation period in such a case than by a high fat maintenance diet furnishing only 70 to 80 grams of total carbohydrate.

If this patient is now put upon a typical moderate protein, moderate fat diet of P. 100, F. 100, the caloric requirement will rise to about 1900 calories, the calories supplied will be about 1300, and the deficit of 600 calories, made up by the combustion of tissue protein, will raise the total P. to 250 gm. and the total available C. will then be 155 gm., still twice as great as would be furnished by the high fat, low protein diet. If we take into account the loss in physical capacity and earning ability involved in undernutrition, as well as the physical discomfort and distress constantly impelling the patient toward violation of the diet, we must conclude that the doctrine of increased carbohydrate tolerance in undernutrition needs to be convincingly proved before the patient should be subjected to this plan of treatment.

The question as to the most favorable weight level for these patients is not always easily determined. Obesity is to be avoided, and probably a weight slightly below the average for the height, age, and sex is the optimum.

While the obese patient should be reduced, we believe it better first to clear up the glycosuria on a high-fat maintenance

diet for the reason, as stated above, that it is more difficult to render the urine sugar free when tissue protein is being burned.

For the same reason we do not use starvation periods even in initiating treatment. The routine maintenance diet is given at the beginning. If glycosuria continues on this diet the tolerance is estimated, and from this a decision is arrived at whether to reduce further the carbohydrate and protein intake or to begin insulin treatment.

The presence of small amounts of diacetic acid and acetone in the urine is compatible with a normal alkali reserve and does not call for a reduction in fat intake.

The question of quantitative versus qualitative diets has points of advantage on both sides. Unquestionably the less restricted a patient is as to the amounts of food he is permitted to take, the less likely he will be to take food outside his diet, and in mild cases the qualitative diet alone may be quite satisfactory. Nevertheless we believe that a definitely prescribed diet has a most important psychologic effect; in addition, it permits even the mild diabetic to eat larger amounts of the carbohydrate foods than he could otherwise, while in the moderate and severe cases it is impossible to achieve satisfactory results without quantitatively prescribing the protein and fat allowances as well as the carbohydrate. We have had experience with both methods, and we believe that even with the closest restriction patients are more likely to adhere to their diets with quantitative feeding, so long as a maintenance diet and sufficient bulk are given; unquestionably the patient is far more impressed with the importance of his diet than he is when he is given only a list of forbidden and permitted foods.

Calculation of the Diet.—Protein.—In the severe case the protein allowance is that necessary to maintain N. equilibrium at its lowest level or about 0.5 or 0.6 gm. per kilogram body weight. With greater tolerance up to 1 gm. may be given, and we use approximately this amount in our routine diet, or about 60 gm. for a patient of average size.

Carbohydrate.—This depends upon the tolerance. In the routine diet the 3 per cent. vegetables are allowed without

restriction. The patient takes from 1 to 2 pounds a day, yielding from 15 to 30 gm. C. If tolerance is low a portion of the vegetables taken must be thrice boiled.

Fat is prescribed in quantity to make up a maintenance diet unless the patient is overweight.

If 50 gm. or 200 calories of P. are given, and 25 gm. or 100 calories of C., it will be seen that for the patient of average size about 1600 or 1700 fat calories will be called for, equivalent to about 190 gm. of fat. This is ordinarily prescribed as follows:

In meat, eggs, and cheese (Table 1).....	44	
Butter, $\frac{1}{4}$ pound.....	110	
Salad oil, 2 tablespoons.....	30	
	<hr/>	
	184	= 1656 calories
Calories from P. and C.....	300	
Calories, total.....	<hr/>	1956

The patient should be instructed to take at least twice daily a bowl of 3 per cent. vegetables with plenty of butter, and salad with oil. There is seldom any difficulty in giving fats in these amounts; when there is, bacon or other fats may be used to help out. If the vegetables and fats are taken at the beginning of the meal there is less likely to be overeating of restricted foods.

The diet instruction sheet which we use is shown in Table 1. This may be used as a qualitative low carbohydrate diet or, by using the marginal spaces, a quantitative diet may be prescribed. The basic diet as usually given is shown in the table. The carbohydrate value of this diet, according to the amount of vegetables taken, is from 15 to 30 gm., protein about 60 and fat 184. The total available carbohydrate is 15 to 30 plus, 0.58×60 plus, 0.10×184 or 68 to 83 gm., according to the amount of vegetables taken.

It will be noted that the only foods prescribed quantitatively on this diet are meat, eggs, butter, oil, and cheese. These foods lend themselves easily to measurement and are fairly constant in composition; moreover, they are universally used and may be prepared in many different ways. On the back

TABLE 1
DEPARTMENT OF METABOLISM
VANDERBILT CLINIC

Amsterdam Avenue and 60th Street

No. 22

New York City

Strict observance of your diet is the most important part of the treatment. Keep this list with you, and follow it exactly. Restrain your appetite. Do not overeat, even of the foods allowed.

Do Not Eat:

SUGAR—In any form or foods with sugar in them.

FLOUR—Of any kind, or foods prepared with flour. Therefore NO BREAD OF ANY KIND IS ALLOWED. No toast, crackers, biscuits, or cakes, no macaroni, spaghetti, etc. No matzoths. No "diabetic" flours or bread of any kind unless so directed.

CEREALS—Of any kind, including oatmeal, rice, tapioca, barley, farina, etc. FRUITS—Of any kind, fresh, preserved, or dried, or jams or jellies made from fruits.

THE FOLLOWING VEGETABLES—Potatoes, peas, beans (except string beans or wax beans), corn, carrots, beets, parsnips, squash, artichokes, dandelion greens, onions (except boiled), turnips, green peppers.

LIVER, OYSTERS, CLAMS, SCALLOPS.

NUTS, except Brazil or butternuts.

Do Not Drink:

MILK—In any form, fresh, sour, or fermented. This includes buttermilk and cream.

CHOCOLATE or cocoa, except cocoa made from cracked cocoa (cocoa nibs).

BEER or malt liquors of any sort. wine, sweet or sour; liqueurs, syrups, etc. FRUIT JUICES and other soft drinks.

May Take:

NOTE—NO FLOUR OR MILK TO BE USED IN PREPARATION OF FOODS OR SAUCES.

All you want { SOUPS—Clear meat soup, broth or bouillon. No vegetables or anything else to be added.
COFFEE AND TEA—Sweetened with saccharine if desired, without milk or cream. Cocoa made from cocoa-nibs.
VEGETABLES AND SALADS—Asparagus, string beans or wax beans, brussels sprouts, cabbage, cauliflower, celery, cucumbers, egg-plant, kale, lettuce, ripe olives, boiled onions, rhubarb, radishes, sauerkraut, spinach, tomatoes, endive, kohlrabi, leeks, dill-pickles, pumpkin, swiss chard.
1/4 lb. BUTTER..... 2 tablespoons OIL..... LARD.....
1/4 lb. MEAT OR FISH—Of any kind, fresh, smoked, or cured, except liver and shell-fish.
2 EGGS.
2 oz. CHEESE—All kinds.
NUTS—Brazil or butternuts only.
DESSERTS—Jellies made from unsweetened gelatin or agar-agar, flavored with saccharine and sourwine, brandy, coffee, or unsweetened flavoring extracts.
CONDIMENTS—Pepper, salt, mustard, oil, vinegar, saccharine, etc.
WATERS—Plain or carbonated.

Special Orders:

of the diet sheet (Table 2) are suggestions for the approximate estimation of portions of these foods. With a little practice the patient can judge the size of a portion with sufficient accuracy without scales.

TABLE 2

Learn to estimate in ounces the size of every portion of food you take, and keep the record on your diet report. It is especially important to know the quantities of the following foods. In order to learn to estimate the portions follow the suggestions given.

MEAT. Have the butcher weigh out a quarter of a pound (4 ounces) of lean meat and note its size before and after cooking.

CHEESE. Have it weighed at the store.

BUTTER. A flat tablespoonful is about half an ounce.

OIL. Half an ounce to the tablespoon.

MILK. Sixteen ounces to the pint. A glassful is 6 to 8 ounces, depending upon the size of the glass.

BREAD. One ounce is a slice half an inch thick and about 3 inches square.

There are 8 teaspoons or 2 tablespoons of fluid in 1 ounce.

If you are allowed any extra starch or sugar you may take it in the form of bread, or you may substitute for the bread, if you wish, other foods in the quantities shown below:

For Each Slice or Ounce of Bread, One of the Following:

Apple, 1 medium	Plums, 2 small	Buttermilk, 16 oz.
Baked apple, $\frac{1}{2}$ large	Fresh pineapple, 3 slices	Cream, 10 oz.
Banana, 1 medium	Dried apricots, 3 large	Potato, $\frac{1}{2}$ medium
Cantaloupe, $\frac{3}{4}$	Unseeded Biscuits, 3	Artichoke, 1 medium
Cherries, $\frac{1}{2}$ lb.	Vienna roll, $\frac{1}{2}$	Beets, 6 tblsp.
Berries, $\frac{1}{2}$ lb.	Flour, 1 tablespoon	Carrots, 6 tblsp.
Grape-fruit, $\frac{1}{2}$ large	Shredded Wheat	Lima beans, $1\frac{1}{2}$ tblsp.
Grape-fruit, 1 small	Biscuits, $\frac{3}{4}$	Green peas, $3\frac{1}{2}$ tblsp.
Grapes, 3 oz.	Flaked cereal, 5 tblsp.	Squash, 2 tblsp.
Lemons, 2 medium	Cooked oatmeal, 3 tblsp.	Turnips, 3 tblsp.
Orange, 1 small	Cooked farina, 3 tblsp.	Almonds, 40
Orange, $\frac{1}{2}$ large	Cooked rice, 3 tblsp.	Brazil nuts, 30
Peaches, $1\frac{1}{2}$ medium	Cooked macaroni, 3 tblsp.	Peanuts, 40
Pear, 1 small	Whole milk, 10 oz.	Pecan nuts, 25
		Walnuts, 20

It must be remembered that even with weighing the accurate quantitative estimation of foods is impossible; variations in the natural compositions of foods, in water content after cooking, etc., prevent more than a rough approximation, but with reasonable care on the part of the patient the result is sufficiently accurate for the purpose of the diet. The patient soon acquires the habit of seeing his food in terms of ounces.

In the calculation of the diets the accompanying table of approximate food values (Table 3) is of assistance. It permits rapid calculation and facilitates the work of the physician.

TABLE 3
APPROXIMATE FOOD VALUES

	Carbohydrate.		Protein.		Fat.	
	Per cent.	Grams.	Per cent.	Grams.	Per cent.	Grams.
Lean meats.	0	0	20	24 per $\frac{1}{4}$ lb.	10	12 per $\frac{1}{4}$ lb.
Fish.....	0	0	20	24 per $\frac{1}{4}$ lb.	5	6 per $\frac{1}{4}$ lb.
Cheese, American.	0	0	30	10 per oz.	30	10 per oz.
Cheese, cottage....	4	1 per oz.	20	6 per oz.	0	0
Eggs, one....		0		6		6
Milk.....	5	1.5 per oz.	3	1 per oz.	4	1 per oz.
Cream.....	5	1.5 per oz.	3	1 per oz.	20	6 per oz.
Butter.....	0		0		90	
Bread, 1 slice, 1 oz..		16		3		0
Green vege- tables....	3	15 per lb.	1	5 per lb.	0	

The patient is given a diet report sheet on which he fills out in detail his diet for the two or three days preceding his return to the clinic. A sample of the mixed and measured urine for the previous twenty-four hours is also brought. Usually an experimental week on the routine diet clears up the glycosuria; if it fails to do so, and the evidence shows that the diet has been adhered to, the tolerance is estimated from the twenty-four hour sugar output as compared with the total available carbohydrate of the diet for the twenty-four hours. If the diet was of doubtful maintenance value the possibility of extra sugar from the combustion of body protein must be taken into account, and a comparison of urea excretion with the estimated protein intake for the twenty-four hours may furnish evidence of this. In addition, if excessive glycosuria casts doubt upon the accuracy or veracity of the diet report, a check may be made as follows: The total reported carbohydrate plus 10 per cent. of the reported fat is subtracted from the glucose excreted. The remainder must come from the protein metabolized. The amount of this

protein is shown by the total urea nitrogen of the twenty-four-hour urine, and the sugar which is formed from this protein is 3.65 times the nitrogen. If no sugar is burned, all of it being excreted in the urine, the ratio of sugar to nitrogen (D : N ratio) will then be 3.65, and any ratio much above this is certain evidence of carbohydrate ingestion above the amount reported. In mild or moderate cases, of course, the ratio should be much lower, so that a high ratio shows a severe diabetes or unreported carbohydrate intake.

If the tolerance is found to be low the protein may be reduced to 0.5 or 0.6 gm. per kilogram body weight, and a part of the vegetable allowance may be desugared by boiling in three waters. If this fails to overcome the glycosuria, or if such a régime proves too difficult for the patient, the use of insulin is indicated.

In those cases which become sugar free at once it is best, unless the case is a very mild one, to continue the basic diet for a few weeks in order to favor the restitution of a higher degree of tolerance and to accustom the patient to proper dietary habits. A gradual increase in the carbohydrate allowance is then begun, usually at the rate of 8 or 10 grams at a time, at intervals of from one to three weeks. Bread or fruit is usually most desired, and on the back of the diet instruction sheet (Table 2) is a table of bread equivalents in terms of fruits, milk, cereals, etc.; if the patient is intelligent and shows a good degree of interest and co-operation he may be permitted to make substitutions from this list according to his own desire.

Under these circumstances when sugar reappears in the urine it will usually be in concentration of less than $\frac{1}{2}$ per cent. It is wise, especially in long-standing or severe cases, to determine the sugar threshold level by blood-sugar estimations. In such cases the threshold is often above 200 mg. and occasionally above 300 mg., and glycosuria cannot then be used as the criterion of a satisfactory diet.

Contrary to the practice of some writers, we do not believe in permitting the patient to test his own urine for sugar unless exceptional circumstances make this necessary. Patients who

examine their own urine are likely to experiment with their diets and keep constantly on the edge of glycosuria instead of well within their tolerance. In our experience control is more adequate if the diet is laid down simply but rigidly. For this reason the use of compounded dishes and "diabetic" recipes is undesirable, and our patients seldom use them. The simple foods permitted on the list are not only adequate and satisfactory to the patient, but are undoubtedly better for the digestion and general health than the complex foods so often recommended in diabetic dietaries.

Special diabetic foods are unnecessary. Cellulose breads are apparently harmless, but do not add appreciably to the tastefulness of the diet, and our patients do not seem to care for them. A few use bran muffins, and if some flour is permissible it may be made to go further in this way.

Casein flours are capable of much misuse and are not of much advantage when used properly. A 2-ounce box of casein flour contains 48 grams of protein, and the 3 eggs used with it in the preparation of the bread add 18 grams, a total of 66 grams, with a glycogenic value of 38 grams of glucose. We have had numbers of patients whose glycosuria cleared up when the excessive protein intake resulting from the use of casein and egg bread was eliminated; of the patients who are able to tolerate this extra sugar we have seen none who would not prefer to have it in the form of $2\frac{1}{2}$ slices of white or whole wheat bread daily.

Insulin.—The use of insulin has been so thoroughly covered in recent literature that little can be added here. When it is indicated, as described above, the patient or a member of his household is instructed in the method of administration, and the dosage is determined by the tolerance and the total available carbohydrate of the diet prescribed. We wish to emphasize here only the uselessness and danger of haphazard insulin administration without previous determination of the carbohydrate tolerance; we also believe in the necessity of a preliminary course of quantitative restriction without insulin in order to fix the patient in the habit of rigid quantitative ob-

servance of his diet. Under these circumstances a high degree of co-operation is the rule, and the results obtained are excellent. This most valuable adjuvant has already established its place firmly; nevertheless, far from replacing dietary treatment, it has served to emphasize still more strongly the necessity of a rigidly controlled diet. It is with this in mind that we have outlined the system in use in our clinic as being adapted by its simplicity to the work of the practitioner in treating diabetes.

CLINIC OF DR. A. L. HOLLAND

NEW YORK HOSPITAL

POSTPYLORIC ULCER: ETIOLOGY, SYMPTOMS, DIAGNOSIS, TREATMENT

BEFORE taking up the cases that we have gathered together for today's clinic, I will rapidly go over some of the important points in the etiology, symptomatology, and the methods of examination involved in the diagnosis of gastric and duodenal ulcer.

Owing to improved diagnostic technic, to the intensive study of gastro-intestinal diseases in large special clinics, and particularly to the co-operation of surgeons, pathologists, and internists, postpyloric ulcer has come to be recognized as a very common disease. It seems to occur about five times oftener than gastric ulcer. For this reason I have selected postpyloric ulcer as the subject for this clinic. I call it postpyloric ulcer rather than duodenal, as I feel that these lesions should be thought of as pyloric affairs. Rarely are they found far distant from the pyloric valve; in fact, the largest percentage of them actually impinge upon the pyloric opening. It is the involvement of the tissues of this important valve to which we owe the regularity of the symptoms presented in this disease. In a fluoroscopic shadow or x-ray plate a stomach without its cap (duodenal bulb) is incomplete. In the etiology of ulcer of the pars pylorica the muscular activity of the antrum and valve itself play an important part, if not in the actual beginning of the disease, at least as a factor which prevents healing. Overaction of these parts is no doubt indirectly responsible for many recurrences. It is, therefore, only proper to identify these lesions with the pylorus rather than with the intestine.

You are all no doubt familiar with the recent theories of ulcer etiology; the older conceptions had more to do with trauma, thermic and chemical agents, high acid, and to autodigestion. We are as yet not in a position to entirely discard any of these as factors; some of them may have a bearing occasionally. It has, however, been fairly well established that in focal infection—teeth, tonsils, antri, etc.—and infections secondary to constitutional infections, such as acute nasopharyngeal disease, lie a part at least of the etiologic secret in a large percentage of the cases. Whether it comes about through bacterial emboli or through the selective affinity of particular organisms for these tissues, such as the streptococcus which Rosenow has suggested, it is not possible to state positively. The latter is the more probable in view of the findings in this important investigation. You will probably remember that Rosenow in 1921 through animal experiments demonstrated this elective localizing power of streptococci that had been obtained from known ulcers. Nakamura (*Annals of Surgery*, January, 1924) has confirmed these findings in the following manner: Of 66 rabbits inoculated with strains from the tonsils of patients known to have gastric ulcers, 46, or 70 per cent., developed definite ulcer or hemorrhage. A streptococcus similar to that found in the pus of patients' tonsils was isolated from both the hemorrhagic and ulcerative areas in the stomachs of the rabbits.

There are very few clinicians who now give high acid any place in the etiology of this disease. High acid appears to be secondary in the ulcer irritation, to the spasm, and embarrassed motility that accompanies ulcer. High acid does not even seem to be the cause of the pain in ulcer, as it can be demonstrated that pain is just as severe and regular in onset where acid is lacking. The onset of pain in postpyloric ulcer does not correspond to the high point of the acid curve, but to that time when the pars pylorica are most concerned in motor activity.

There is another element in ulcer etiology—neurotrophic deficiencies must be considered; in fact, I am inclined to feel that these disturbances, this neurotrophic imbalance, antedates the actual infection and round-cell activity in ulcer. In other

words, ulcer is a fatigue disorder, in which the breakdown of the neurotrophic mechanism of the parts involved makes possible an infection. I know of no other chronic disease in which the onset of the acute exacerbations so regularly follows fatigue or long-continued emotional strains. In pursuing any plan of treatment, therefore, this phase of the disease must be reckoned with.

Symptoms.—The symptoms of postpyloric ulcer are particularly regular when compared to those of other diseases. There are, of course, irregular cases, and then, too, a regular syndrome may be interfered with through the manifestations of symptoms due to a coincident disease such as gall-bladder disease or appendicitis. But in the vast majority of postpyloric ulcer cases a pain, usually a gnawing, grinding, burning, or boring distress, is complained of, and this distress nearly always has a definite relation to the taking of food. It usually begins two to three hours after the usual American breakfast, three to four hours after a moderately hearty luncheon, from six to seven hours after a full dinner (night pains). The pain of postpyloric ulcer usually continues until the next meal unless relieved by an alkali.

Heavy meals seem to postpone the pain longer than the lighter ones, but when it does occur it is more severe than after the light meals. It will be seen that when the heavy meal is taken in the middle of the day, afternoon pain is not usually experienced, the light supper being taken in time to head it off. But in this case the distress comes earlier in the evening, usually before the patient retires. Ulcer patients do not always complain of a definite pain. The sensation may be simply that of excessive hunger or a pressure; occasionally it may be translated by the patient as a nausea. Whatever the indigestion symptom may be, it occurs in this same regular relation to the meals.

In gastric ulcer the pain is just as regular in onset in relation to the meal, but it, as a rule, occurs much earlier in the digestive cycle. The nearer such a lesion is placed to the pyloric valve, the nearer will the pain onset coincide with that of the postpyloric syndrome. In gastric ulcers placed well up on the lesser

curvature the pain occurs very soon after eating—from one-half to one hour—probably because the muscular activity of the stomach in this zone is at its height from one-half to one hour after eating, but with a lesion of the pars pylorica the onset of the pain is coincident with the increased muscular activity that occurs when the last portions of the meal are being propelled through the pyloric opening, and continues through the spasm of the empty stomach. If you will observe fluoroscopically the stomach of a patient suffering from postpyloric ulcer, a light barium meal having been given, you will see that the thin portions of the meal will pass off almost at once, but if you will add to that meal pieces of meat, say 2 cm. square, you will see that these pieces of meat drop to the bottom of the stomach, where they will remain until the very last. If they have not been dissolved by this time they will be pushed up and grasped by the antrum and forced through the reluctant pyloric opening, in this way causing a severe spasm. This is the time for the onset of pain in this form of ulcer. If at this same time a portion of the stomach contents is aspirated through a small tube, it will usually be seen that the acid is lower than it had been one hour after the meal.

Pain in active ulcer does occur where the foods are soft or even fluid. The intense spasm that immediately follows the emptying of the meal is here the cause. If high acid is not the cause of ulcer pain, why does the neutralization of the acid relieve such distress? It has been shown that the hydrochloric acid of the gastric juice causes through direct action and also probably as a hormone the closure of the pylorus, and it thus excites pylorospasm and antralspasm. The neutralization of the acid results in a relaxing of this spasm, and therefore a lowering of the tension, with consequent relief of pain. Food acts in the same way by diluting the acid.

There is another interesting point concerning the pain of ulcer. With gastric ulcer the pain occurs relatively soon after a meal, but when the stomach is really empty it is spontaneously relieved. But in ulcer of the pars pylorica the pain occurs later and remains until the next meal. Where in ulcer a distress is

felt in the epigastrium continuously, a soreness, for instance, it is usually found at operation that the lesion has penetrated to the serous coat, or at least the inflammation has involved it. If this more or less constant soreness is relieved by pressure on the epigastrium or by change in posture from the erect to the supine or prone, it would indicate formation of adhesions involving neighboring structures. In a large percentage of postpyloric cases the pain is reflected back.

Periodicity is a most valuable symptom in ulcer. It is very much more noticeable in postpyloric ulcer than in the gastric variety. Attacks of indigestion that occur at fairly regular times with complete relief between such attacks are very suggestive of ulcer, even though the character of the distress or the symptoms may not be classical. In some cases, many, in fact, there is a seasonal periodicity; that is, attacks will regularly occur in the fall or winter or perhaps early spring. This occurs so frequently during the cold months that it has been suggested that these lesions are reinfected through the respiratory tract.

Belching, regurgitations, and other irregular gastro-intestinal symptoms are not so common in ulcer. Nausea and vomiting may occur, but usually only because of delayed motility through persistent pylorospasm or actual obstruction. In gastric ulcer nausea and vomiting are perhaps somewhat more common than in the pyloric affairs. This is probably due to a secondary gastritis. Where vomiting does occur because of obstruction it relieves the pain for a while. Where the vomiting results from irritation within the stomach, pain is not relieved so completely; in fact, it may even be increased by the act.

The appetite is rarely impaired. In fact, it is usually increased, although the patient may hesitate to eat because of the resulting pain. The bowels are apt to be constipated. The health in general is rarely affected except where excessive dieting has been indulged in or where hemorrhage has been a feature causing secondary anemia. When fainting attacks are complained of one should think of hemorrhage; this is not infrequently the first and only sign of a severe hemorrhage.

Physical Examination.—There is very little in the physical examination of these patients that helps in diagnosis. It is, of course, essential that a very thorough examination be made. It is surprising how frequently the indigestion secondary to disease of the chest—an old pleurisy, for instance, or a fibroid phthisis—will simulate gastric or duodenal ulcer. And then one should hunt very thoroughly for possible foci of infection.

The most constant sign in the abdominal examination is the tenderness on pressure in the midepigastrium. This rarely coincides with the actual location of the lesion. It is one of those reflex phenomena that are so common in abdominal lesions. In a fairly large percentage of these cases there is also a tender point just to the right of the tenth dorsal vertebra. This is lower and nearer the spine than the tender posterior point that one so frequently finds in gall-bladder disease.

Gastric Analysis.—In gastric analysis we have a valuable aid. A large percentage of such ulcers give high acid values, higher in pyloric and postpyloric ulcer than in those well up on the stomach wall. But the findings of gastric analysis are in no way diagnostic. As a routine we now use in this hospital the Ewald one-hour extraction. I believe the information thus obtained is more usable than the findings of the fractional method, and it is certainly a less complicated procedure, and this must be considered in a busy service.

The character of the returns, irrespective of the acid values, is important in differential diagnosis. The hypersecretion type—nearly all clear fluid—tells of spasm without actual obstruction, and therefore is more common in reflex gastric irritation, such as in chronic appendicitis. The retention type is seen where the specimen in a cylinder arranges itself into three layers, the topmost being made up of disintegrated and fermenting food masses and mucus, the middle a turbid fluid, and the bottom a more or less normal looking mass of contents. As its name implies, this return of a test-meal suggests some obstruction. The normal type of return, that in which the fluid and food masses divide about equally in the cylinder, is the type most often seen in ulcer without obstruction. Occult

blood in the gastric return is of no significance, but where it is persistently found in the feces, with the patient on a hemoglobin-free diet, it is significant.

It is, I think, safe to say that at least 70 per cent. of postpyloric ulcers can be diagnosed through a well-taken history, and the balance of them by means of the x-ray, particularly the fluoroscope. In the gastric lesions the fluoroscope and x-ray films are about equally valuable, but in postpyloric ulcer the fluoroscope is essential. It is only through the manipulation and pressure that the operator exerts upon the abdominal wall that the duodenal bulb can be properly filled out, and even then the patient must be turned about at different angles in order to see the shadows properly. This is obviously impossible in taking films, but fluoroscopy requires sharp eyesight, considerable strength, and a good, quick judgment.

QUESTION BY A DOCTOR: Do you use the string test?

ANSWER: We have not used it in this hospital recently. Dr. Conner formerly employed it in the service, and I believe the results at first were fairly good, but not always reliable. We have not used it since employing the fluoroscope in routine. There are many possibilities for error in the string test; one cannot be sure of the exact location of the ulcer by this means; $\frac{1}{4}$ to $\frac{1}{2}$ inch difference in the site of a lesion may make considerable difference not only in the diagnosis but also in the treatment. It will, I believe, usually show the presence of ulceration, but I have never been able to tell by this means if an ulcer was prepyloric, pyloric, or postpyloric. I believe that Dr. Ewing and other pathologists are right who do not think that ulcer is very often transformed into cancer, but at the same time I can never be sure that a lesion on this side of the pyloric valve is a simple ulcer or a cancer, and for this reason alone I would condemn this test. Gastric ulcer (and I, of course, include in this prepyloric ulcer), I believe, belongs to the surgeons. On the other hand, cancer does not occur in the duodenum, or so rarely that it does not count. The treatment of this type of ulcer, therefore, should remain the physician's problem unless obstruction is a feature or there is persistent bleeding. A mere diagnosis of

ulcer is no longer sufficient. That is easy. Strings and stomach-tubes will only help to confirm an ulcer history. Our problem is very much more complicated. By a skilful use of the flu roscope and the correct interpretation of x-ray films we must decide just where the ulcer is, how much induration has taken place, and the effect the lesion has upon the motility of the stomach and duodenum. It is also essential to know of penetration and of the presence of secondary adhesions.

To illustrate some of these points in diagnosis I will rapidly go over the cases of these patients who have presented themselves. I will dwell only on the essentials, but please remember that nothing of any importance has been omitted in the preparation of the cases, in the history taking, examinations, or tests.

Mr. F. is thirty years of age, a native American, for the past six years a seaman in the Navy. There is nothing of interest in his family history, habits, or previous history, except in the latter a tendency to frequent colds and tonsillitis. About twelve years ago he remembers that he would occasionally notice a burning sensation in the epigastrium. This would occur several times a day and was usually relieved by food. He thinks this indigestion would last several weeks, followed by relief for a month or two. It was never severe. He did not consult a doctor until about a year ago, when the attacks became severe. The pain was then of a boring character and there was considerable tenderness in the midepigastrium. It regularly occurred from three to four hours after breakfast and lunch, and would waken him at 1 or 2 A. M.; always relieved by food or by soda. The first severe attack followed shortly after an attack of tonsillitis. The three subsequent attacks have all occurred in the cold weather, but he is not sure that they have been related to head colds or to tonsillitis.

On physical examination we find a very tender point in the midepigastrium, but nothing else of any importance. The tonsils are large and cryptic, but not at present inflamed. A one-hour Ewald test showed a return of 45 c.c., normal type; total acid 100, free HCl 70; no occult blood.

The fluoroscope showed a normal stomach, but a characteristically deformed duodenal bulb, probably much indurated, but with no evidence of stasis. The fluoroscopic series was otherwise negative.

The diagnosis in this case is evident, and the indication for treatment quite plain. While we cannot hope to effect any change in his ulcer through removal of the tonsils at this time, we should nevertheless lose no time in having it done to prevent recurrences through that channel. He has already been placed

on the diet, which I will later discuss with you. He has also been taking a neutralizing powder—magnesium carbonate, sodium bicarbonate, and bismuth subcarbonate, of each equal quantities by weight—a teaspoonful of this combination an hour after every meal.

He tells us that he has had no symptoms since the second day of this very simple treatment. He was not inclined to follow a calisthenic course that was prescribed, as he had been told that the slightest strain might bring on a hemorrhage, but he is now doing so and is feeling perfectly well, is back at his very strenuous duties, and we hope he will remain at work.

There is no indication for surgery in this case. The stomach empties perfectly, and if we can by a regulation of his hygiene and habits prevent recurrences, the induration in the walls of the bulb will subside and he will probably remain well.

As a contrast I will ask you to consider our next case:

Mr. C., an American, thirty-eight years of age, a mechanic, came to us last spring complaining of a distress in the umbilical region. He describes it as a soreness, occasionally a burning pain, relieved by hot water and soda and occasionally by food, but not always. It occurred some time after the meals, but not always regularly. He thinks it was usually about two hours after eating, but occasionally much later. The onset he places at about two years previous to his first call. He had before this enjoyed fairly good digestive health, but with a tendency to constipation. His family history, habits, and previous history are practically negative. A fluoroscopic examination resulted in a diagnosis of prepyloric ulcer with involvement of the pylorus and duodenal bulb. It was thought that adhesions were responsible for most of the postpyloric defects. x-Ray films confirmed these findings. There was no evidence of retention.

Gastric analysis gave high acid values; total 80, free HCl 62; no occult blood.

There was nothing in the physical examination of interest except the tenderness on pressure in the midepigastrium.

The patient improved on the regular ambulatory ulcer diet and neutralizing powder, but his progress was not as satisfactory as we had hoped for, and with the prepyloric involvement in mind it was finally decided to submit him to operation. The surgeon confirmed the diagnosis at the operating-table. The gross appearance was certainly that of a simple indurated

pyloric ulcer with adhesions involving the duodenum, but the laboratory returned a report of early carcinoma. This explained the somewhat irregular symptoms presented. It is illustrative of our limits in diagnosis, and clearly points to our responsibility in dealing with lesions that are diagnosed as gastric. The patient has apparently recovered from the pyloric resection that was performed and there is every reason to expect a cure.

QUESTION BY A DOCTOR: You say that the mere diagnosis of ulcer is easy. I can understand that, but will you tell me how I can deal with this question of medical treatment versus surgery. I practice in a community many miles from a hospital and x-ray plant, and most of my patients are too poor to avail themselves of this aid to diagnosis.

ANSWER: The responsibility of diagnosing and caring for an ulcer patient without the aid of the x-ray is a heavy one, and yet one can use reasonable safeguards. As I have already said, the history is of prime importance. In order to make sure of the relation of pain to meals, which is so important, it has been found convenient to have the patient keep a diary in which he notes each day the time of each meal and the character of the food eaten, and to carefully indicate the exact time that the pain begins, how long it lasts, and in what manner relief is obtained. This is good as a start and may be all that is necessary to differentiate a gastric from a postpyloric lesion. But please do be careful with the neurasthenics; such intensive introspection may easily be the starting-point in mental invalidism. The careful interpretation of gastric analysis is also called for. The necessary technic for the use of the tube is not difficult. If I were situated as you are, I believe I should use the string test also, but with due regard for its limitations. And then, without seriously jeopardizing your patient's interests, a therapeutic test for a month or six weeks will help considerably. But remember that rest in bed will frequently give at least temporary relief in early cancer as well as ulcer. I prefer to have these patients pursue their regular routine of living except as to the diet and neutralizing medication. In a case that has presented the classic postpyloric ulcer syndrome in

which freedom from symptoms has immediately followed the adoption of this plan, I should continue without thought of further investigation. But where you know there is ulceration and the symptoms have been more or less irregular and do not promptly respond, I would strongly advise that you impress upon the patient the necessity of more complete investigation than your community can offer. I would not consider age in these cases. We see many cases of cancer in those comparatively young.

The next 3 cases have been diagnosed as postpyloric ulcers. The patients all give practically the same sort of history—pain two to three hours after meals and at night, relieved by food and alkalis. α -Ray plates and the fluoroscope have confirmed. Gastric analysis in each case has shown relatively high acid values. I will not bore you with the details. I am showing them to you to illustrate the benefits of simple hygienic regulation. Not one of these patients has lost a day from business. They are all gaining in weight and, as you see, look perfectly well. Their tonsils will be watched for evidence of disease and removed if necessary. The nose and throat department will be asked to exclude the antri. Where apical abscesses are found, teeth will be sacrificed. The grinding function of the teeth will receive appropriate attention. In our anxiety to remove foci of infection I fear we are inclined to disregard this very important function. In advising replacements, remember that a metal grinding surface is one-fifth less efficient than porcelain as a food mill.

Except for mineral oil when it is indicated, and the neutralizing powder already mentioned, these patients receive no medication. Very rarely we use $\frac{1}{100}$ grain of atropin sulphate three times a day between meals for excessive spasm, but $\frac{1}{4}$ grain of luminal will be found just as effective and better tolerated by most patients. The principle of the diet is soft, non-stimulating food taken at frequent intervals. Small doses—1 teaspoonful of olive oil just before each meal is a useful adjuvant; it seems to soothe; it inhibits somewhat the appetite juice, and as this part of the juice acts as a hormone for the true juice, probably limits the whole output somewhat.

The appended diet list is the one we advise for business people. There are many foods that can be added to this that come within the requirements. As progress is made such a diet can be extended to include the tender meats, but never any tough fibrous material, uncooked fruits (except those mentioned), or uncooked vegetables. Rest for a few minutes before and after meals is a great help. Perhaps the greatest boon that these patients can receive is the assurance that their trouble is understood, that they are not in imminent danger of perforation or hemorrhage. The cases of perforation and hemorrhage are in a different class; they seem to come out of a clear sky with little or no previous history such as these patients have related.

The patients should be made to understand that each recurrence brought about through a disregard of the rules will bring them nearer to the time when a gastro-enterostomy will be necessary because of obstruction through accumulated induration and scar tissue.

AMBULATORY ULCER DIET LIST

Morning:

A teaspoonful of olive oil fifteen minutes before eating.

One or two tablespoonfuls of stewed fruit, or a baked or steamed apple without skin or core, or a sliced scraped banana, all with cream and a little sugar.

A cup of cocoa or hot malted milk or a glass of milk.

A saucer of any thoroughly cooked breakfast cereal with milk or cream and sugar.

One soft-boiled egg.

A piece of toast with butter.

Two hours after breakfast a glass of milk, buttermilk, or malted milk.

Noon:

A teaspoonful of olive oil fifteen minutes before eating. A sandwich made of white bread without crust of sardines (in oil not mustard), or pot cheese and jelly, or minced chicken or salmon, or any fresh minced fish, or

A portion of creamed sweetbreads or broiled brains.

White bread with butter.

A banana, cream puff or éclair, or any soft sweet pudding.

Two hours after luncheon a glass of milk, buttermilk, malted milk, hot chocolate, or a dish of vanilla or chocolate ice-cream.

Evening:

A teaspoonful of olive oil fifteen minutes before eating.

A cream soup, thoroughly strained, made of corn, cauliflower, celery, lettuce, spinach, dried peas, dried beans, potatoes, or mushrooms.

Two soft-boiled or poached eggs.

A tablespoonful of mashed potato and any fresh green vegetable mashed, strained, and creamed, or any thoroughly cooked breakfast cereal.

White bread with butter.

Stewed fruit with cream, gelatin with cream, cream puff, éclair, a dish of vanilla or chocolate ice-cream, or any soft sweet pudding.

At bedtime a glass of milk, buttermilk, or a cup of cocoa.

Do not eat or drink anything that is not mentioned in this list.

Use no seasoning except a sprinkle of salt.

Use no rich sauces or gravies and no soups made with meat or meat stock.

All food must be soft, the vegetables thoroughly mashed, and when possible strained.

Eat slowly. Chew all food thoroughly. Hold each mouthful long enough in the mouth for the saliva to become thoroughly mixed with the food before swallowing. Even the liquids should be held in the mouth for a short time before they are swallowed.

Do not smoke.

Do not drink alcohol of any kind.

The teeth should be put in perfect condition, all cavities filled, and artificial teeth placed where the natural ones are missing.

When possible, rest for fifteen minutes to one-half hour before and after eating.



CLINIC OF DR. HAROLD E. B. PARDEE

NEW YORK HOSPITAL

THE EXAMINATION OF CARDIAC PATIENTS

THE diagnosis of cardiac disease has come to depend upon the results of many different methods of examination. Accordingly, I believe it is worth while to discuss the relative importance of the information obtained in these various ways, and to indicate how the numerous findings can be boiled down to a clear and comprehensive diagnosis which will be of service in the treatment of the patient.

A proper diagnosis will include the cause of the disease and whether or not it is still active. It will include the extent of involvement of the heart tissues and the effect of this involvement upon the rhythm of the heart and upon its ability to carry on the circulation. We must also know whether or not there are conditions in other organs which might embarrass the heart in carrying on its function, or which might produce the symptoms that annoy the patient.

It is plain that our investigation should be most thorough. It should include a careful history of the patient's complaints from the beginning of his illness to the present. Each symptom should be obtained in such detail that we know its exact character, what may increase its severity, what may alleviate it, and what associated symptoms may be present. In many cases the history has a diagnostic importance quite equal to that of the physical examination, and in some its importance is greater.

As to the physical examination, this must be equally comprehensive. It must never stop with an examination of the heart, pulse, and arteries, but should include the lungs, abdominal organs, extremities, nasopharynx, eye and tendon

reflexes, superficial lymph-nodes, and such other special examinations as are suggested by the history or the other physical findings. This detailed examination will establish the fact that the patient has no other disease that might cause the symptoms, and will often help much in deciding on the etiology of the heart condition. By a correlation of the results of such a history and such a physical examination we may expect to arrive at a proper understanding of our patient.

In order to illustrate some of these points I will present to you a patient with heart disease.

A man thirty-four years of age, a theatrical producer, who knows of no childhood diseases except measles. At sixteen years of age he had an attack of rheumatic fever which he was told left him with valvular disease. He had no symptoms from this either at school or at college. He took part in athletics without restriction, playing baseball and basketball in match games. He did not feel that his wind was less good, or his endurance less, than that of his friends. After leaving college his life did not include much physical activity, but there were frequent late parties with a free use of alcohol and tobacco. During the last five or six years he often noticed for a day or so after such parties that his heart thumped heavily, and if it did this frequently he would have a sense of shortness of breath. Sometimes he would have a dry cough on the day following the parties. He attributed the cough to smoking and the exhaustion was considered as a "hangover," so that he did not go to a physician about these symptoms. For three or four years he has been unable to lie on the left side without the appearance of a thumping sensation in the heart region. Ordinarily, however, he was not troubled by the thumping. He was able to walk about freely on the level, to walk up ordinary grades, and to climb two or three flights of stairs without discomfort. During the last two or three years he has found that three flights of stairs would leave him a little more breathless than it used to, but not enough to deter him from climbing them.

Recently he has been for several weeks subjected to late hours, tobacco and alcohol, and irregular meals and sleep. One day after having driven an automobile about 100 miles he felt unusually fatigued and noticed frequent thumping of his heart and a dry hacking cough without pain in the chest. Next morning he awoke with a severe cough and felt distinctly short of breath most of the time. He remained about the house that day, the symptoms continuing, and that evening he raised some bloody sputum, and was kept awake by shortness of breath, having to sit up in bed most of the night. The next day he came to the hospital for treatment.

The etiologic factor of the heart disease appears quite plain in this case, for after an attack of rheumatic fever he was

found to have a valvular damage. Such a plain relation cannot always be established. It is common, especially in women, to find valvular disease where neither a history of a rheumatic attack, nor of chorea, nor of any of the minor etiologic conditions, such as tonsillitis, frequent sore throats, or muscle and joint pains which are allied to rheumatic fever, can be obtained. If I may use the term "rheumatic infection" as applying to the cause of all of these conditions, it seems as though this infection, perhaps entering through the mucous membrane of the tonsil or throat, had special affinities in the brain, causing chorea; in the muscles, causing muscle pains; in the joints, causing rheumatic fever or lesser joint pains; in the heart valves, causing the various types of valvular disease; or in the heart muscle, causing a certain type of myocardial disease.

So then, if a certain rheumatic infection affects the joints and the heart, rheumatic fever and valvular disease result. In another patient the brain and heart may be selected by the poison, and chorea and valvular disease will be found. Other patients still may have only joint symptoms, or only chorea, or only valvular disease, so that it clearly is not necessary to find a definite history of one of the rheumatic infections before deciding that the patient has rheumatic valvular disease. If there is valvular disease at all, and if syphilis and arteriosclerosis can be excluded as causes, it is fair enough to conclude that there is a rheumatic basis.

An important factor in any history is the patient's attitude toward his symptoms, whether he notes them carefully, exaggerates them, or disregards them. This patient tends to disregard his symptoms, so that when he says that he was short of breath it is likely that dyspnea was severe. It is common for patients with lesser degrees of dyspnea to fail to recognize it as such, and to speak as did this patient, of a sense of fatigue, or exhaustion, or weakness. This is especially true with children, who very rarely say they are short of breath on exertion, but say that they are tired.

Dyspnea is a symptom which should be elicited in great detail, for when it appears with exertion it is an important

symptom of cardiac insufficiency. In the lesser grades of decompensation it is noticed only upon unusual effort, as after climbing three flights of stairs or upon walking up a hill or on running. It gives rise to a limitation of the patient's former ability to exercise. Only when cardiac insufficiency is marked does dyspnea appear when walking on the level at an ordinary rate, or on climbing one flight of stairs. If the patient cannot lie down without shortness of breath it represents an advanced grade of heart failure. Our patient, it will be noted, was not troubled by dyspnea after three flights of stairs until the last two or three years, thus showing that his cardiac reserve was not seriously impaired, but that it was gradually lessening.

Another type of dyspnea which this patient exhibited is due to the heart beating with an abnormal mechanism. In his case a thumping of the heart due to premature beats was noticed, independent of exertion. If this palpitation was more marked than usual it would give him a sense of dyspnea. Not all patients with premature beats have this sensation, but a few of them do so.

A sense of the heart beating rapidly is commonly felt on effort. This more usual type of palpitation was not complained of by this patient, who felt only the thumping of his premature beats. In certain patients the palpitation of rapid heart action is so prominent that it takes the place of dyspnea as the limiting sensation on exertion. Such patients are usually of the nervous type and keenly conscious of all their sensations, so that when palpitation rather than dyspnea is the limiting symptom there is not usually a serious degree of cardiac failure. Palpitation may verge into a sensation of dull pain when severe, and there are some patients who develop pain from the same things that ordinarily produce palpitation. These differences depend upon variations in the sensory mechanism of different individuals.

Pain is an important symptom of cardiac disease, though not shown by the patient under discussion. It is a peculiar symptom, varying greatly in its character with the causative condition. It is often due to an abnormal mechanism of the heart-beat, an abnormal rhythm of one sort or another, such as

premature beats or tachycardia. When due to this cause, even though it may be very severe, it has not the serious import that it has when arising from structural changes in the heart, though this heart may have a normal rhythm.

The subject of precordial pain is a difficult one to discuss within the time limits of this clinic, for so many details of the pain and its associated signs and symptoms are important in the diagnosis. The subject has been fully discussed in a former clinic,¹ when it was the chief topic. Now it is considered only as one of many symptoms of heart disease and must be kept in its properly subordinate place. A dull pain described as heavy or pressing, coming on with exertion and disappearing promptly with rest, centering about the region of the lower third of the sternum, though perhaps radiating variously about this level and typically down the left arm, is nearly always a pain due to serious cardiac disease from arteriosclerosis of the coronary arteries. If the pain centers higher, above the level of the third intercostal space, it is more likely to arise from aortitis. In both cases the pain is likely to be accompanied by an eructation of gas. Pains of a sharp sticking character, especially if their central location is in the region of the apex-beat, are not apt to be due to serious cardiac disease, no matter what their severity or how typical of so-called angina their area of radiation may be.

The cough which this patient complained of on the days when he felt weak and exhausted was, in all probability, due to pulmonary congestion. The cough with bloody sputum which developed with the final attack was certainly due to this.

Edema of the ankles is a common symptom of heart failure which was not complained of by this patient. Edema does not appear when failure is slight, but with moderate degrees of failure it appears about the ankles or shoe tops at the end of the day, and disappears again over night. It is very variable in different patients and is often absent when, judging by the severity of the other symptoms, there would be every expectation of

¹ Med. Clin. North Amer., March, 1921, Disease of the Coronary Arteries, Pardee, H. E. B.

its being found. It is more likely to be found in older than in younger patients, and for the same grade of decompensation more likely in those who have long had symptoms than in those who have developed symptoms recently.

See now what a good picture of this patient the history above has developed. He has had heart disease for many years. The causative rheumatic infection has apparently ceased to be active. Until lately his ability to exercise has been quite normal. Periods of abuse, however, have been followed by mild symptoms of cardiac insufficiency, but lately he has noted a slight, constant limitation of his ability to exercise. Quite recently he had severe symptoms of cardiac failure which have brought him to bed.

What are the physical signs developed by examination?

On admission his appearance was practically as you see him now except that now he can lie down with comfort and then could not on account of a sense of suffocation. Now he can move about freely in bed without discomfort, but then he developed evident dyspnea as a result of any movement of the body. His lips and finger-nails were slightly cyanotic then, but this has cleared up.

At present his pulse is 80 per minute, regular, full and strong, somewhat collapsing. The arterial wall is slightly thickened. The blood-pressure is 160/60. The pulsation of the carotid arteries shows rather more plainly than normal. The neck veins are not distended as he sits erect and do not show a systolic pulsation. The arm veins collapse when at the level of the second rib, showing that there is no back pressure in the right auricle.

The chest shows no deformity and moves normally with respiration. The lung areas give no abnormal dulness and no abnormalities of breath or voice sounds. On the first examination, however, there were many râles heard at both bases posteriorly, especially on the right side, where they were heard well around into the axilla and as high as the angle of the scapula. At that time there was also congestion of the neck veins, showing back pressure in the right auricle.

The heart gives a strong heaving impulse in the fifth and

sixth spaces almost as far to the left as the anterior axillary line. Dulness extends 4 cm. to the right in the fourth intercostal space. In the second intercostal space the dulness due to the great vessels has a width of 7.5 cm. The first sound at the apex is obscured by a plain, but not loud blowing systolic murmur, and following the second sound is a plain long rumbling diastolic murmur. A plain blowing diastolic murmur is heard all over the base and body of the heart, loudest along the left border of the sternum at the level of the third and fourth interspaces. There is a loud rough systolic murmur heard best at the aortic area. The second sound is loud at the aortic area. At the first examination it was still louder at the pulmonic area, but is not so at present. The abdomen is normal in appearance. The liver dulness extends 8 cm. below the costal margin in the mid-clavicular line; its edge is not felt. The spleen is not palpable. On admission the liver was larger and the edge somewhat firm and tender.

The extremities show no edema, and did not on admission. The ocular and deep tendon reflexes are normal. The teeth and tonsils appear normal. The superficial lymph-nodes are not enlarged and those of the neck especially are normal. The urine is normal at present, but on admission showed a definite trace of albumin, numerous hyaline and finely granular casts, and a specific gravity of 1028.

The hemoglobin and red blood-cells are normal. The Wassermann reaction was negative.

An x-ray picture of the heart (Fig. 52) shows it to be greatly enlarged and confirms the clinical observation of a normal width of the aortic arch.

An electrocardiogram (Fig. 53) shows left ventricular predominance by the small R and deep S in Lead 3, with R smaller in Lead 2 than in Lead 1. There is also an abnormality of the T-wave in Lead 1, it being a downward deflection instead of upward, as it should be, and there is notching of the Q R S group in Leads 1 and 3. These two abnormalities, of Q R S and of T are to be considered as an indication of disease of the ventricular muscle.

The features of this physical examination which might have a bearing upon etiology are the condition of the tonsils and teeth and their respective lymph-nodes. If they were evidently diseased we might think that the cardiac infection had entered through this portal, but there was no evidence of disease found here. However, having in mind the clear evidence of rheumatic

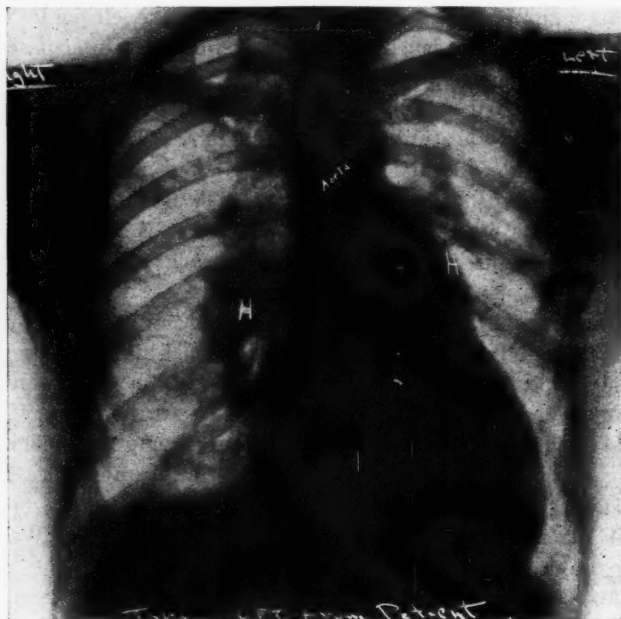


Fig. 52.—x-Ray photograph of the patient, the plate being 6 feet from the patient. Note the large heart, the small aorta, and the dense shadows at the lung hilus (H) due to congestion of the veins.

infection shown in the history, we have a special interest in the teeth and tonsils, for they often serve as portals of reinfection through which the already damaged heart receives a further injury. In all patients with valvular disease these organs must be carefully scanned to make sure that they are not harboring disease. In this patient there is no sign of it.

The Wassermann reaction is of importance in the etiologic rôle, for it will often indicate that a disease thought to be due to some other cause has a syphilitic origin. This patient's negative Wassermann thus serves to clinch our previous diagnosis of a rheumatic etiology.

The pathologic diagnosis is to be made from the physical examination. Cardiac disease will be found to manifest itself

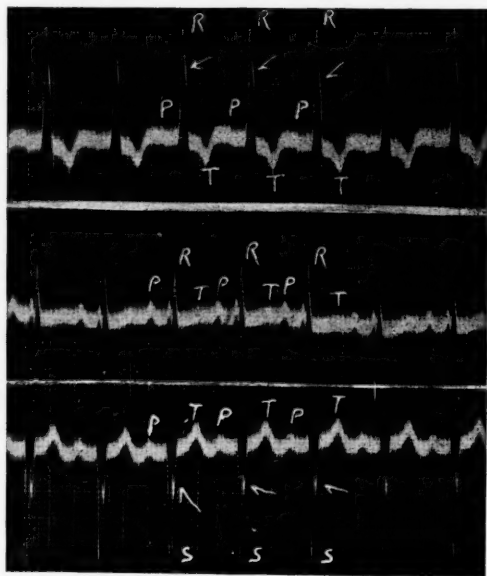


Fig. 53.—The electrocardiogram, Leads 1, 2, 3 from above downward. Note the downward T wave in Lead 1 and the notching of the Q R S group at the points indicated by arrows in Leads 1 and 3.

in three general ways, namely, (1) Evidence of enlargement of the heart, (2) evidence of valvular disease, (3) evidence of disease of the muscle. In addition to these the condition of the aortic arch must be determined, especially in its ascending portion.

Enlargement of the heart or aorta is appreciated by means of percussion, palpation, and the x-ray. If the left border of

cardiac dulness should extend 1.5 or 2 cm. beyond the mid-clavicular line it is good evidence of cardiac enlargement and, of course, the further to the left, the greater the enlargement. If, in addition, a strongly heaving apex impulse is felt, we may be the more certain of enlargement. When there is doubt about the presence or the degree of enlargement it may help to have an x-ray picture of the chest taken with the tube 7 feet from the plate. Slight degrees of cardiac enlargement are more plainly made out by this method than by percussion, and especially so if the lungs are emphysematous.

The distinction as to whether enlargement is due to hypertrophy or to dilatation was formerly thought to be of great importance, and numerous measures were recommended for the differentiation of these conditions. It has come to be realized that none of these measures can distinguish satisfactorily between the two conditions, and attempts to do so have been given up. We now realize that dilatation can only exist for a brief time without hypertrophy, and that hypertrophy always includes a certain degree of dilatation.

The distinction as to which chamber is chiefly responsible for the enlargement is usually of only academic importance. There are times when it may help in the diagnosis of valvular disease, but the distinction cannot be made with certainty by ordinary clinical means. To answer the question properly we must consider the form of the cardiac outline by x-ray and the evidence given by the electrocardiogram as to auricular hypertrophy and right or left ventricular predominance.

Dilatation of the aorta may often be recognized by a widening of the area of dulness in the second intercostal space. Unless this widening is marked an x-ray examination should be made. The fluoroscope is preferable to the plate for this purpose because the patient can be turned so that several oblique views of the aorta can be obtained. It is better to have a plate, however, than to have no x-ray examination at all.

Our patient has a very definite enlargement of the heart, so that the x-ray was really not necessary for corroboration. The x-ray evidence of lack of aortic dilatation is very important in

view of the fact that there is disease of the aortic valve. The lack of aortic involvement suggests that the disease started in the valve and did not arise by an extension of an aortitis. This is further corroboration of a rheumatic etiology, for syphilis commonly involves the coats of the aorta along with the aortic valves.

The diagnosis of the type of valvular disease depends chiefly upon auscultation. In this patient the murmur of aortic insufficiency dominates the picture, and there is also the murmur of mitral insufficiency. The rumbling, diastolic murmur at the apex may be dismissed as a Flint murmur and not due to mitral stenosis, for there are none of the secondary signs of this valve lesion, either the presystolic crescendo murmur or the sharp first heart sound.

The loud rough systolic murmur at the aortic area is difficult to interpret. If a thrill were present it would be proper to consider we were dealing with aortic stenosis, but without the thrill the diagnosis is not so sure. I believe, though, that the patient has this lesion, for he lacks the marked carotid pulsations and the large pulse pressure which would be expected with so well-developed an aortic leakage.

The diagnosis of the heart muscle depends upon the evidence of its functional ability afforded by the patient's symptoms, and upon the character of the electrocardiographic record. Evidence from the character of the heart sounds is quite unreliable, for these are so greatly modified by the condition of the chest wall and lung tissue and by the degree of filling of the ventricles with blood. Heart sounds of a certain character are common with myocardial disease, but are often found when it is not present. The functional ability of the heart, too, is difficult to interpret in terms of disease of the ventricular muscle, for even a good muscle may fail if the valvular disease imposes an insurmountable handicap. A severe stenosis or insufficiency of a valve may make it impossible for the ventricular pump to maintain a sufficient blood flow, and a blood-pressure of 200 or over certainly puts a severe strain upon any heart. Thus it is only in the absence of marked valvular lesions or hyper-

tension that the cardiac function is more than an approximate guide to the condition of the myocardium.

The electrocardiographic record gives the best information of the ventricular muscle which is obtainable. There are certain abnormalities of the ventricular waves which are recognized as being the result of disease of the muscle of these chambers. Either notching of the Q R S group or a downward T-wave, alone or in various combinations, and often with a prolonged duration of Q R S also, are the special features of the record that indicate the presence of myocardial disease. They are present when the disease has a certain extent, or, with a lesser extent, a certain situation in the ventricular muscle. It is likely that a minimal amount of disease may exist without changing the Q R S and T waves. It is unlikely, though, that an amount incapable of changing these waves would give rise to failure of the function of the muscle.

Our patient has two significant abnormalities of the electrocardiogram, a downward T wave in Lead 1, and notching of the Q R S group in two leads, so that we may fairly conclude that his ventricular muscle is diseased. In considering the heart's functional ability, however, we find that in spite of what seems to be a marked valvular lesion, the heart was able to carry on the circulation at least fairly well. He was able to walk on level ground without dyspnea and to climb two flights of stairs without discomfort. This is probably explained in part by the tremendous hypertrophy the heart has undergone. Though the muscle is diseased, there is a tremendous amount of it, so that its driving power may not be so deficient as its quality.

We have now completed the pathologic diagnosis, having found a normal aorta, a greatly enlarged heart with disease of the aortic valve leading to insufficiency and slight stenosis. There is also mitral insufficiency and a damaged ventricular myocardium.

There remains the diagnosis of the pathologic physiology. Has the rhythm of the heart been affected, and what is the degree of its functional impairment?

We have said that the heart-beat is irregular. Feeling the pulse we note occasional long pauses which suggest dropped beats, but listening at the apex of the heart we find that these apparent dropped beats are due to premature beats of the heart with dropped pulse beats. The electrocardiogram confirms the fact that there are premature beats and indicates that they have a ventricular origin.

The interpretation of the significance of premature beats is not easy. Sometimes they are quite benign, arising from nervous causes quite outside the heart, and bear no indication of cardiac disease. On other occasions they are a sign of digitalis poisoning, and on others, as probably here, a sign of the irritability of an overstrained muscle which must expend its utmost effort to carry on the circulation. The mere observation of premature beats has no real import, but the interpretation of their cause in the light of the whole clinical picture is of great clinical value. In this patient it is a sign of strain, and suggests that the heart is near the edge of severe decompensation. Even without this evidence of overstrain afforded by the abnormal rhythm we should still know that the heart's reserve force is impaired. We know this in part from the history of a limitation of the patient's activities by dyspnea. He says that he was able, before this attack, to walk on level ground without dyspnea and to climb two flights of stairs without discomfort, but the third flight winded him. He is, however, a man who tends to minimize his complaints. I venture to say that he does not walk as fast as many do, and that if you could have examined him after two flights of stairs you would have found an unusual degree of dyspnea and a rapid heart. Moreover, these would have taken an unusually long time to pass off.

It is in just such cases, where we suspect that the patient is overstating or understating his ability that a rather strenuous test exercise, such as stair climbing with a 30-foot rise, or swinging a 10 pound dumb-bell twenty-five times from the floor to over the head, will be helpful in deciding what his exercise tolerance may be. We are able to observe him immediately after the exercise and see whether the reaction is excessive in

terms of dyspnea and tachycardia, and we can note whether the return to normal is unduly prolonged. A normal person can do these exercises at a fair rate of speed and show at the end but moderate dyspnea and tachycardia, which give way to normal breathing and normal heart rate within two minutes. This is a normal reaction to the exercise.

A patient who performs this exercise and gives a normal reaction must have a heart with functional ability little if at all impaired. A patient who performs the test exercise and gives an excessive reaction will show more marked dyspnea and tachycardia, with the return to normal delayed to a full two minutes, or beyond it, to three minutes or more. Such a patient has an impaired cardiac function and the degree of impairment may be gaged roughly by the degree of the reaction. In using a test exercise it is not well to put the patient to such a severe strain that he will show an excessive reaction. I do not mean that it is dangerous, for the patient will stop voluntarily before the danger point is reached, but it is decidedly unpleasant for him to find himself, at the end of the exercise, gasping for breath and distressed by an overactive heart. To avoid this we must consider the patient's own account of his limitations when walking or climbing stairs, and must watch him during the test exercise, having him stop it as soon as he begins to show objective dyspnea. It is in this way—by combining the patient's account of his limitations with our own observation of his reaction to exercise—that we arrive at an estimation of the heart's functional ability.

At present the functional ability of this patient's heart is so slight that he should not be given any test exercise. He has just recently had severe cardiac failure, shown by congestion of the lungs with the formation of râles, distention of the neck veins, and orthopnea. He is recovering his cardiac reserve under treatment and in due course of time will again be able to be out of bed and to walk about. At that time it may be advisable to attempt to rate his exercise tolerance by a consideration of what he says he can do without discomfort and of his observed reaction to an exercise test.

This patient, then, to summarize, has cardiac valvular

disease due to a rheumatic infection; the infection is apparently no longer active. The aorta is normal, but the aortic valve is diseased, showing insufficiency and slight stenosis. The mitral valve is also diseased, showing insufficiency. The heart is greatly enlarged and the myocardium is damaged probably by the rheumatic infection which affected the valves or by the series of repeated overstrains to which it has been subjected. The heart is irregular because of premature beats of ventricular origin, probably an evidence of strain. The cardiac compensation was somewhat impaired before the present attack, and with this attack failed severely, so that such extreme signs as orthopnea and engorged neck veins made their appearance. This failure was due to a special period of strain, and so we may expect that, the strain being removed, he will be able to recover almost, if not quite, to the state of compensation that he enjoyed before the attack.

I have tried in reviewing this case to give you an idea of the special importance of each of the different details of the examination, keeping constantly in mind that we must make a complete diagnosis under the four headings—etiology, pathology, abnormal function, and cardiac compensation. We must select from the history such features as have a special bearing on any of these aspects of the diagnosis. The presence of dyspnea and the amount of exertion needed to produce it; the character and exact situation of precordial pain and the circumstances which lead to its appearance; palpitation, edema, chronic cough, and all other symptoms must be analyzed with care and made to yield their full value of information.

We must proceed with the physical examination with the same broad view, not depending upon any one feature for more than a small part of the diagnosis and prognosis. The loudness and the character of the murmurs is important, the character of any irregularity is important, marked enlargement is important, electrocardiographic abnormalities give important evidence of the condition of the myocardium, an estimation of the degree of cardiac reserve at the time of examination is important; but upon no one of these things can a diagnosis be founded

nor a prognosis be made. When, however, they are combined into one composition along the lines I have tried to indicate we shall have reached an understanding of the patient which will amply repay us for the trouble we have taken and which will place our treatment on a thoroughly sound basis.

CONTRIBUTION BY DR. WALDEN E. MUNS¹

NEW YORK CITY

DISTURBANCES OF HEART ACTION

Introduction.—In 1628 Harvey declared that the circulation of the blood in the body depended upon the continuous contractual function of the heart. Even prior to that time the study of the pulse as an indicator of disease was practised. It was recognized that certain diseases and certain conditions of the body resulted in disturbances in the rate and rhythm of the pulse, as noted in the radial artery or in the pulsations of the neck. It was not long before the watch was being widely used to determine the behavior of the heart under varying conditions.

In certain ways the heart has been one of the organs most easily studied because of the accessibility of the arterial pulsations which result from cardiac systole. It has been only within late years, however, that the heart muscle itself, the center of circulatory power, has come under minute observation.

In 1856 Kueliker and Müller first demonstrated a current of action in the heart. After dissecting out the gastrocnemius muscle with its nerve from the leg of a frog, the excised nerve was laid along the surface of a contracting heart. With each contraction of the cardiac muscle the frog muscle would also contract, thus demonstrating some kind of a current of action to be present in the heart.

Sanderson and Page in 1880 showed this current of action in the beating heart to be an electric potential change in the organ, as they were able to demonstrate with a crude form of rheotome and a galvanometer in 1887. Waller showed that it was possible to register the electric changes of the human heart-beat, using a clumsy capillary electrometer.

¹ The case records and electrocardiograms cited in this paper are from the Cardiac Clinic of the New York Post-Graduate Medical School and Hospital, Dr. Robert H. Halsey, Director.

In 1892 Bayliss and Starling made the first graphic study of the contracting heart of the male human. For ten years after the work of Bayliss and Starling little information was given to the scientific work regarding heart function, but during this interval Eintoven had been perfecting a form of string galvanometer that could be used to record graphically the electric changes in the contracting heart. The instrument evolved in this work—the electrocardiograph, with certain improvements—is used to this day. The facility with which it may be used and the precision of the curves obtained with it have caused it to

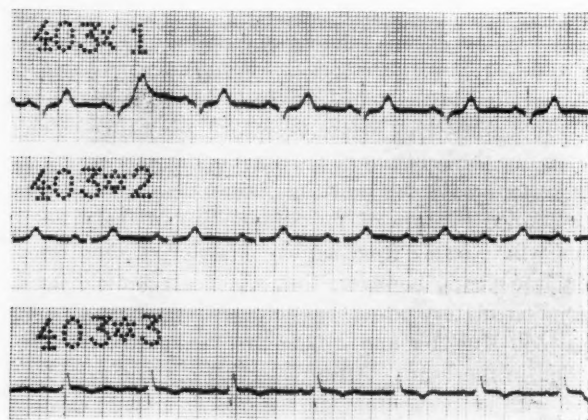


Fig. 54.—Normal electrocardiogram.

supersede all other forms of galvanometer, and has brought the systematic examination of hearts within the field of practical medicine. In order to understand the mechanism of heart action in health and under conditions of disease it is necessary to keep in mind the special anatomy of the heart and the unusual and characteristic physiology of heart muscle.

Special Anatomy.—The sino-auricular node was discovered by Keith and Flack in 1907. It is a mass of tissue lying at the junction of the superior vena cava and the right auricle, and has a liberal blood-supply from a central artery. The mass is com-

posed of fibrous tissue in which are embedded muscle-fibers, nerve-fibers, and nerve-cells. The nerve-cells and fibers connect on either side with the sympathetic and the vagal trunks.

There is complete functional and anatomic connection between the auricles and ventricles. The auricular-ventricular node lies at the edge of the auricular tissue, at the posterior and right border of the septum, and is composed of collected fibers from the auricle. The auricular-ventricular bundle (bundle of His) begins at the auricular-ventricular node and

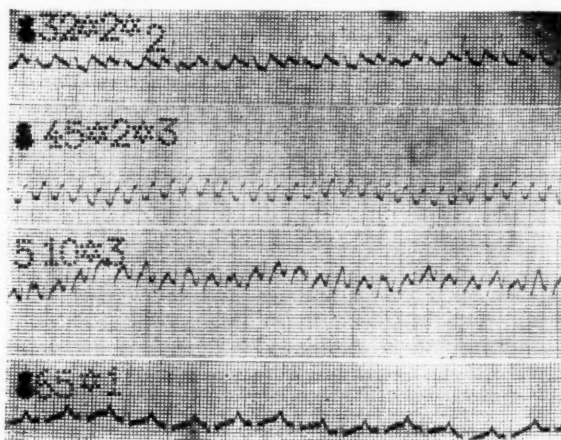


Fig. 55.—Fast rates: 832, Auricular flutter. 845, Paroxysmal tachycardia supraventricular in origin. 510, Tachycardia ventricular in origin. 865, Simple tachycardia.

runs forward and downward to the beginning of the septum, where it divides into right and left branches. These branches divide into smaller branches as they travel down the sides of the septum, and finally arborize into very small fibrous bands. These, in turn, divide into the subendocardial net of Purkinje fibers. From the Purkinje fibers the direct communication with the ventricular fibers takes place.

The sino-auricular node is the source of the contraction impulses, and is often called the "pace-maker" of the heart.

The contraction impulses from the pace-maker flow downward to the auricles, through the walls of the auricles to the functional tissues between the auricles and the ventricles, and then, in turn, through these elements of the conduction system to the ventricular muscle-fibers. The heart rate and the fundamental rhythm of the heart are dependent upon the function of the

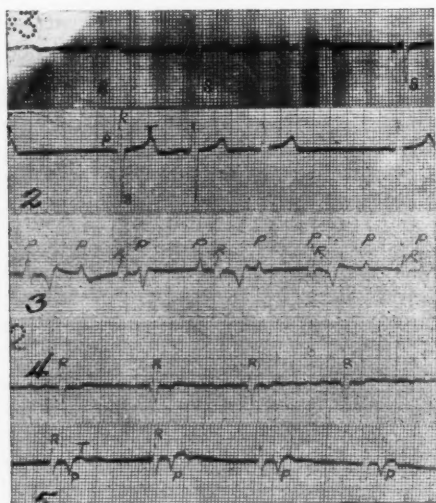


Fig. 56.—Slow rates: 1, Simple bradycardia, representing normal auricular-ventricular sequence following retrograde rhythm noted in 5 below. 2, Sino-auricular block slow heart. 3, Complete auricular-ventricular block slow ventricle. 4, Slow ventricle in auricular fibrillation with a-v block. 5, Retrograde rhythm slow ventricle.

pace-maker, and are, to some extent, modified by conditions of the lower fibers of the system.

Physiology.—In common with smooth and skeletal muscles cardiac muscle possesses the attributes of irritability, conductivity, contractivity, and tonicity. It differs from all other muscle tissue in four ways: first, any stimulus strong enough to reach the threshold of irritability is followed by a maximum contraction of all the muscle-fibers of the heart. This characteristic

is referred to as the "all or none" law. Second, the function of cardiac muscle is automatic. The normal heart contraction is due to contraction impulses arising in the sino-auricular node. A failure of the node to supply contraction impulses that are strong enough to reach the threshold of ventricular irritability results in the automatic formation of contraction impulses in some new center, such as the auricular-ventricular node, and to a lesser extent in the bundle of His and its chief branches. Third, the contraction of heart muscle is rhythmic. Contraction

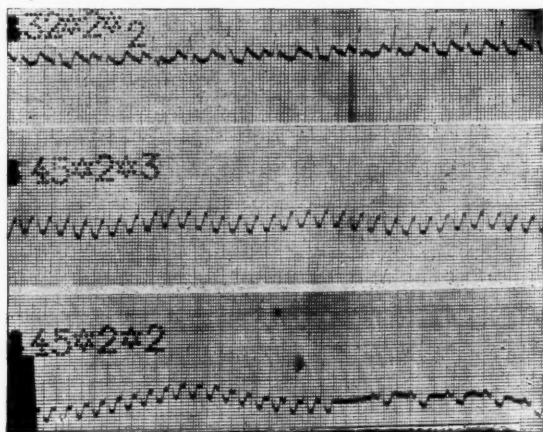


Fig. 57.—832, Auricular flutter. 845, Paroxysmal tachycardia supraventricular in origin showing abrupt termination of the fast rate.

impulses from the normal pace-maker of the heart are delivered rhythmically. When these fail and automatic impulses arise in some other region of the heart, the impulses from the new center are also rhythmic, the rate depending upon the region of their origin. Except the normal respiratory changes in rhythm, nothing but conduction disturbances will change the fundamental rhythm of the heart. Fourth, there is a "refractory period" in cardiac muscle contraction during which time the muscle-fibers are not irritable. A normal contraction impulse coming into the ventricular at this time is not followed by

contraction. This condition results in a limitation of ventricular rate and is a safety measure. This characteristic of heart muscle also explains the occurrence of the "compensatory pause" following premature ventricular systoles. The characteristics of maximal contraction with minimal stimulus, and the loss of irritability during the refractory period, provide that there can be no "summation" of cardiac muscle contraction.

The "Typing" of Cases.—The simplest and easiest method of approach to an understanding of the various disturbances of

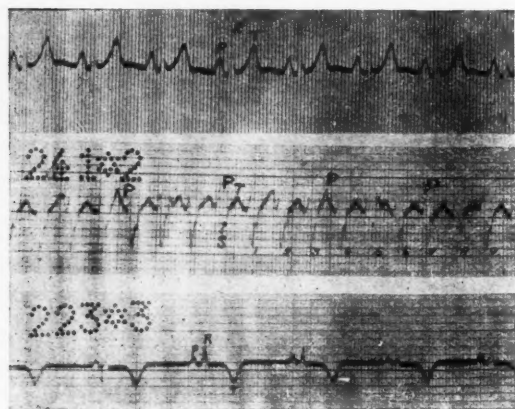


Fig. 58.—Top, Electrocardiogram before paroxysm. 241, Electrocardiogram during paroxysm of tachycardia ventricular in origin. 223, Electrocardiogram of same case after digitalis therapy.

heart action is the study of the abnormal mechanism that underlies each type of disturbance. It is not sufficient to refer to a very fast heart as tachycardia, unless proper study of the case has eliminated the other types of fast rates. To call an irregular heart action an arrhythmia is to leave the exact diagnosis of the condition as much in doubt as before the words were spoken.

Various forms of disturbed heart rate and changed heart rhythm are seen in almost all acute infections, and, indeed, in many chronic conditions where the clinical diagnosis does

not in any special way refer to the heart. The diagnosis of Basedow's disease does carry with it a certain understanding that there is a disturbance of heart action, but there are several types of rate disturbances, anyone of which may appear.

The occurrence of unusual heart rates and rhythm in infections and chronic conditions does not necessarily mean permanent or grave heart affection. In individuals suffering only

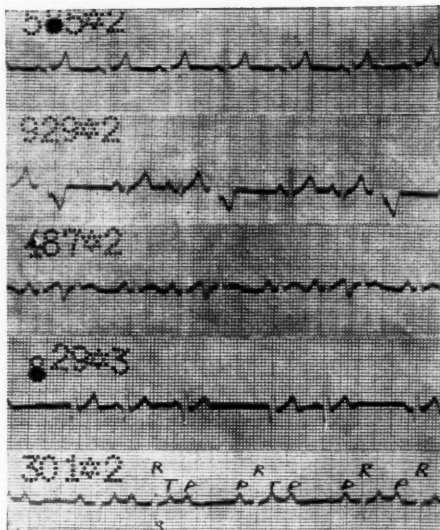


Fig. 59.—Intermissions: 585, Normal electrocardiogram. 929, Premature ventricular contraction. 487, Premature auricular contraction. 829, Sino-auricular block. 301, Complete a-v block with dissociation of auricle and ventricle.

from heart disease the disturbed heart action may be the first sign of the infection. In terminal conditions of heart affections most of the cases show disturbances of rate or rhythm.

The "typing" of the case is accomplished through clinical observation and the use of the polygram and the electrocardiogram. Such typing helps in making a proper prognosis. That treatment of the heart condition depends to some extent upon such typing will be shown below.

Classification According to Mechanism

Fast rates:

Simple tachycardia.

Paroxysmal tachycardia:

Supraventricular in origin.

Ventricular in origin.

Auricular flutter. May be paroxysmal.

Auricular fibrillation. May be paroxysmal.

Slow rates:

Simple Bradycardia.

Heart-block:

Sino-auricular.

Auricular-ventricular.

Arrhythmias:

Sinus in origin.

Auricular fibrillation.

Intermissions:

Premature contractions.

Sino-auricular block.

Auricular-ventricular block.

Alternation.

FAST RATES

Simple tachycardia, or ordinary fast heart, is the most common occurrence of all forms of rate changes. The heart rates vary from 120 to 150 per minute. The fast rates are present most of the time and vary somewhat with exercise, excitement, emotion, etc. The slower form of this type of fast rate is presented in acute infections with temperature elevations, and the fast rates are noticed in asthenic conditions seen during the convalescence from severe illness, in patients with marked nervous background, and in such cases of chronic intoxications as are represented by hyperthyroidism.

The rhythm is not disturbed except for the occurrence of sinus arrhythmia, the rate increasing on inspiration and decreasing on expiration. When the breath is held, the rate is constant. In the case of acute infections recovery of normal

heart rate follows the termination of the infection and the subsidence of the temperature. Simple tachycardia from the other causes noted tends to disappear with removal of the cause and the improvement of the general health.

Electrocardiographic study shows a normal sequence between auricles and ventricles, with the contraction impulses arising in the normal location—the sino-auricular node.

Paroxysmal tachycardia may be defined as that type of fast heart rate which begins and terminates abruptly. The paroxysms

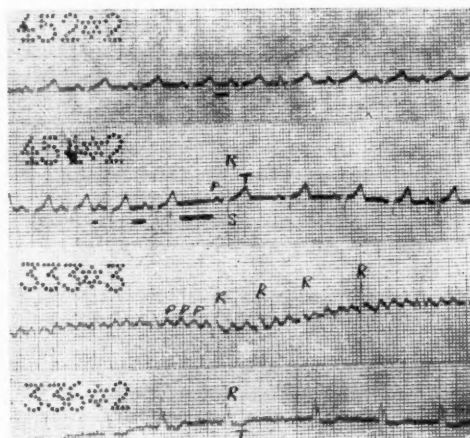


Fig. 60.—Arrhythmias: 452, Normal electrocardiogram. 454, Sinus arrhythmia. 333, Impure auricular flutter (auricular fibrillation). 336, Auricular fibrillation.

may last for a few moments, a few hours, or for a few days. In exceptional cases the duration of the attack may continue into weeks. The commonest occurrences are of paroxysms lasting for a few moments or hours. The general causes are the same as those noted above. Among the conditions associated with recurring paroxysms of tachycardia the most prominent are hyperthyroidism, instability of the nervous system, and the condition formerly known as "effort syndrome," and now called a "neurocirculatory asthenia." There are cases where,

from the standpoint of pathology, the affection stands as a definite entity, no amount of laboratory or clinical study sufficing to reveal toxic or other causes.

One of the strangest things in connection with the paroxysm is the haphazard and diversified stimuli that provoke or terminate this attack. The patient may be sitting quietly in a chair, and the slamming of a door will mark the beginning of a paroxysm that may last for hours or days. Any small crisis in daily life, any undue excitement or emotion, sudden changes in the posture of the body, dashing cold water in the face, may

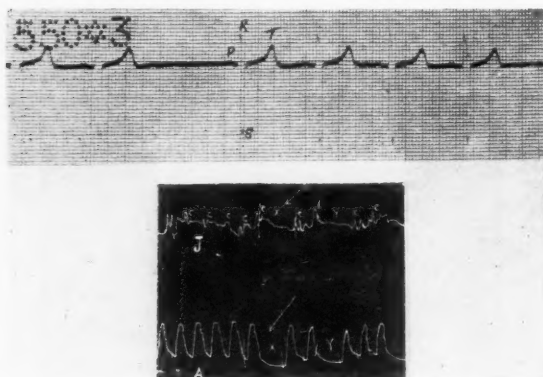


Fig. 61.—550, Electrocardiogram of sino-auricular block. Below, polygram of same case. Note that during arterial intermission there are no waves in the jugular pulse.

bring on an attack, and the sudden cessation of the attack may follow stimuli identical with those of the beginning.

The rhythm is characteristically regular and the rate is usually from 150 to 200 beats per minute.

The shorter attacks or paroxysms do not produce super-sensitive sensations beyond palpitation of the heart, flushing of the face, and a feeling of unstable equilibrium, but when they first appear they inspire fear of impending death. The long-continued attacks cause great distress. The patient suffers from palpitation, throbbing in the head, dizziness, and, finally,

great weakness. There is a scared and anxious expression on the face. The respirations are labored. The face is engorged and edema of the ankles may be present. The pulse is soft and of a rapidity difficult to count. The ventricular rate usually corresponds with the radial pulse-rate and the heart sounds are short and tapping in quality, and may be less distinct than normal. The heart may become dilated. After the termination of an attack the symptoms disappear and the patient rapidly becomes comfortable.

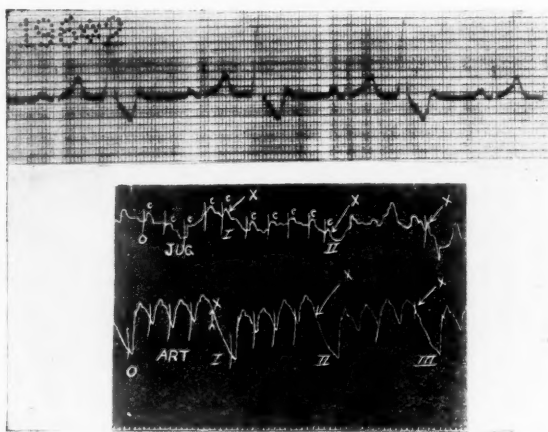


Fig. 62.—196, Electrocardiogram showing premature ventricular contractions. Below, polygram of same case. Note that during arterial intermission a "c" wave appears in the jugular pulse, denoting ventricular systole.

Electrocardiographic study of patients during paroxysms reveal the source of the abnormal contraction impulses to be in the auricular in most cases, and in the ventricular in a few cases, and in the atrioventricular area in exceptional cases.

The attack begins as a premature contraction and repeats itself in rapid succession until the abrupt termination. As the source of the aberrant impulses is supraventricular, there is no alteration in the deflections of the ventricular complex, but these normal complexes are preceded by irregular auricular deflections of anomalous outline.

If the new rate is a response to impulses from within the ventricle, the ventricular type of complex prevails. At the abrupt termination of the paroxysm a normal compensatory pause follows the last abnormal contraction, after which the normal rate and rhythm of the heart ensues.

The treatment of paroxysmal tachycardia consists in the removal of the cause. During attacks the patient should be kept in bed, where he will assume the position most comfortable, whether it will be one of reclining on one side or sitting propped

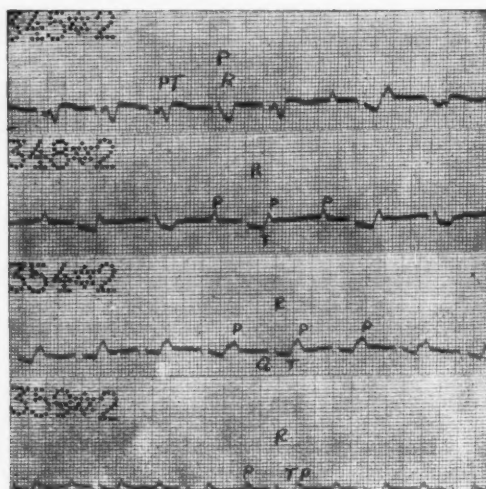


Fig. 63.—Block from digitalis: 345, Ventricular intermission due to exceptional long auricular-ventricular time interval (.52 second). 348, The block has become complete (dissociation of auricle and ventricle). 354, Recovery phase same case (P-R interval .48 second). 359, Same case with P-R interval of .28 second.

up against pillows. He should be in a quiet room with a light and bland diet. Catharsis should be as mild as possible. Quietude at night should be enforced, with opiates if necessary.

Pressure on the vagus nerve, preferably the right one, may terminate the attack, but the rate is not slowed by such procedure. Exercise and posture changes will not alter the rate,

but the attack sometimes ceases with the assumption of unusual postures, such as that of the knee-chest position. The supraventricular type of attack is not helped by digitalis. The



Fig. 64.—Arteriograms showing alternating pulse. The top tracing shows alternation only during the first few pulses following a premature ventricular contraction. The lower tracing is that of well-established alternation, but alternation increases following premature ventricular contraction.

individual paroxysm due to impulses ventricular in origin is often cured with digitalis.

As illustrations of the supraventricular and the ventricular types of paroxysmal tachycardia the following cases are reported:

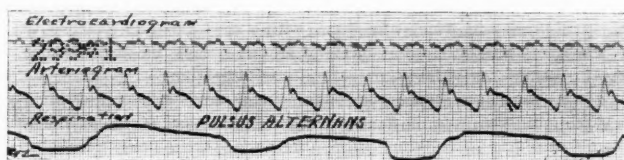


Fig. 65.

Case I.—The patient was a male aged thirty-four years. For the last ten years he had been a street-car motorman. He had never been ill since having some indefinite illness in childhood. He had been particularly hardy and strong, and had never used alcohol or tobacco and denied any venereal infection.

Six years ago he noticed a slight swelling of the neck below the collar, and three years ago the eyes were noticed to be prominent. Within three years he had developed an unusual excitability and nervousness, so that his work as a street-car motorman had become very difficult. Two years ago

he began to suffer palpitation of the heart on the most ordinary exertion, and developed a disposition so worrisome and excitable that he was able to work only spasmodically as an extra man.

He stated that for two years his heart had been acting in a peculiar way. At the smallest excitement, such as an insignificant accident to his car, or during bursts of temper, or on stepping down from his car to the ground with unusual force, the heart began to palpitate. The heart's action would remain very fast from a few minutes to several days, and the attack usually passed off as suddenly as it came. During the last year the heart has become so irritable to slight stimuli that he has been able to bring on attacks of palpitation and fast rate at will, and has, to some extent, been able to stop the attacks usually after a few hours' duration.

On examination it was noticed that the face was suffused with blood, the respirations were rapid, and there was marked exophthalmos. There was an unsteadiness of gait and marked tremor of the hands. There was slight swelling above the inner ends of both clavicles. The radial pulses were rhythmic and soft and so rapid as to defy counting by palpation. The heart dulness extended beyond the midclavicular line to the left. The ventricular impulses were not felt. Auscultation of the lungs revealed moist râles over both bases. The ventricular sounds were almost inaudible, but a faint rapidly repeated fluttering was heard in the fifth left intercostal space.

During the course of the first examination the pulse and ventricular rates suddenly fell to a rate of 96 per minute. The heart sounds did not improve in distinctness.

While the heart was contracting at the slower rate, at the command of the examiner the patient was able to precipitate another attack of fast rate. This he usually did by swallowing rapidly and then holding the breath. Such attacks usually lasted for an hour or so, and the patient was generally able to terminate them by a similar act of swallowing.

Electrocardiographic examination showed the condition to be paroxysmal tachycardia, supraventricular in origin, with a ventricular rate of 246.

The urine showed large amounts of albumin. The blood chemistry was normal. The blood Wassermann reaction was negative.

The diagnosis was substernal goiter. For three days the patient received 10 c.c. of digitalis every three hours, and for six days received 15 c.c. of digitalis three times a day, all without effect. Surgical operation was decided upon, and a substernal colloidal goiter was found and partially removed. Since operation the attacks of paroxysmal tachycardia have become less frequent. The patient is no longer able to stop the attack by the use of methods of swallowing and holding his breath. When paroxysms do occur, there is a tendency for them to remain longer than before the operation.

Case II.—The patient was a male; married, forty-five years of age, weighing 178 pounds; a lawyer by profession. The patient came to the hospital suffering with dyspnea, palpitation, and great weakness. Since childhood there had been no definite illnesses, infections, or surgical operations. For fifteen or sixteen years the patient had had indefinite digestive disturbances, sometimes a feeling of tenseness in the abdomen, local tenderness

in the lower right quadrant of the abdomen, and eructations of gas. At times there had been nausea, and vomiting had been easy to induce. Vomiting had brought relief. Abdominal pain had never been present. For fifteen years the patient had been subject to attacks of palpitation of the heart, lasting at first only a few minutes or a few hours. These attacks began abruptly with the following provocations: eructations of gas, sneezing, turning over in bed, cold wind blowing on the back of the neck, violent closing of the door, outbursts of temper, hurrying for a street car, etc. The paroxysms usually occurred during the periods of digestive disturbances noted above and lasted for from a few moments to three weeks. At first the attacks were of short duration, but for the last three years the duration had become longer, until it reached three weeks. The patient had occasionally been able to bring the attacks to a close by administering to himself a soapsuds enema, and there are records of attacks being cured by assumption of the knee-chest position.

When first seen this patient was suffering extremely with dyspnea, weakness, dizziness, and a pain in the chest. The eyes were prominent, the face a dusky red, the vessels of the neck violently palpitating, the abdomen tense and tympanic. The radial pulses were weak and so rapid as to defy counting. The heart was enlarged to the left and right and the heart sounds were low, indistinct, and fluttering. As with the pulse, counting the ventricular contractions was difficult.

The blood Wassermann was negative and the blood chemistry was normal. The urine showed a marked trace of albumin, with many red blood-cells present.

The patient was put to bed and 5 c.c. of tincture of digitalis was administered in one dose, followed by a dose of 2 c.c. in three hours. Six hours after the initial dose of digitalis the paroxysm abruptly ceased.

Electrocardiographic study revealed the heart condition to be paroxysmal tachycardia of ventricular origin. The diagnosis of the abnormal condition was chronic appendicitis.

After the success of the tincture of digitalis in the first attack in the hospital digitalis was used in all subsequent attacks with success. After four months of unsuccessful general treatment, which included diet, gradual reduction of weight, exercise, and catharsis, operation for chronic appendicitis was decided upon. After the operation the patient did not have an attack of tachycardia for several months. Short paroxysms of several hours' duration occur at the present time, each one being eventually cured with digitalis.

Auricular Flutter.—The condition of auricular flutter is relatively rare, but in any cardiac clinic several new cases are apt to appear each year. The condition occurs under circumstances similar to those of paroxysmal tachycardia, but differs from the latter in mechanism. It is thought to indicate myocardial degeneration.

The auricles contract from 200 to 400 times a minute and the ventricles contract at rates varying from 100 to 200 per

minute. The fast auricular rate is caused by aberrant impulses arising from an irritable center somewhere in the auricle. The ventricular contractions may be one-half, one-third, or one-fourth the number of the auricular contractions. This phenomenon is due to a temporary partial block of the contraction impulses by the auricle and ventricle, the block acting as a compensatory means for shielding the ventricle. A typical phenomenon is the abrupt halving of the fast ventricular rate at the termination of the attacks. The electrocardiogram will show the auricular deflections occurring rapidly and regularly, with the supraventricular complexes occurring one-half, one-third, or one-fourth as fast as the auricular complexes. Definite proportion between auricular and ventricular complexes is the rule, the mechanism differing in this respect from dissociation of auricle and ventricle as seen in auricular-ventricular heart block.

The treatment consists in absolute mental and physical rest, with small doses of opiates to insure sleep. Therapeutic digitalization in some cases will cause the condition of auricular flutter to pass into auricular fibrillation, the latter condition giving way to normal sequence and rhythm. While this response to digitalis is typical, it fails in some cases. Quinidin sulphate has been successfully used in some cases. The patient should be under general hygienic and dietary treatment aimed at a probable myocardial change.

Case III.—The patient was a male, forty-four years of age, a ticket salesman, admitted into the hospital suffering from dyspnea, a pain in the left chest and arm, and headaches. The full history showed diphtheria in infancy, measles at three years of age, chorea at eight years, pneumonia at eight and again at ten years, and acute rheumatic fever at twenty-one years of age. The onset of the cardiac trouble was in 1918, when he suffered from dyspnea on exertion, with coincident pain in the left chest in the region of the heart. The condition improved after three weeks in the hospital. Then, for two years, there was mild suffering from breathlessness, precordial pains, with occasional edema of the legs and ankles. The symptoms gradually grew worse up to the time of his admission to a cardiac clinic, when the whole left arm was involved in the simple complex, sharp pains darting from the precordia to the shoulder and down into the fingers. There were also frequent spells of palpitation with or without exercise, and headache was frequent. Sleep was poor, due to orthopnea.

When first seen the patient was dyspneic, cyanotic, and complained much of the precordial pain. The pulse was intermittent, but not arrhythmic. His weight was 177 pounds and his height 5 feet, 5 inches. The diagnosis at this time was aortic insufficiency, mitral insufficiency, premature contraction of the ventricles, cardiac hypertrophy, and obesity.

The electrocardiogram at this time showed a regular heart with an occasional premature contraction of the ventricle. The first time that the pulse was found to be arrhythmic was six months after the first observation, when the electrocardiogram showed the auricles to be fibrillating. Apparently the fibrillation of the auricles continued for two months, when the symptoms became so severe that the patient went to bed in a hospital. On admission to the hospital the ventricle rate was 144 per minute, arrhythmic, with a radial pulse deficit of 74. Tincture of digitalis was administered, 10 c.c. each day for three days, at the end of which time the ventricular rate was 108 per minute, with a pulse deficit of 14. Tincture of digitalis was continued, 4 c.c. a day for five days. On the fifth day in the hospital, after having received 38 c.c. of tincture of digitalis, the heart regained normal auricular-ventricular sequence, the rate being 80 per minute.

Two months later there was a severe attack of palpitation, with increase in all the usual symptoms. The pulse was weak and very fast. The electrocardiogram showed the condition to be auricular flutter, with an auricular rate of 296 per minute and a ventricular rate of 148 per minute. The patient was given 0.3 gm. of quinodin sulphate three times a day. In four days' time the normal rhythm and rate had returned and remained for ten days. Twice since that time there have been attacks of fast pulse which, in each case, have been relieved by one dose of quinidin sulphate, 0.3 gm.

Auricular Fibrillation.—A description of this condition is given below under the heading of Arrhythmia. Attention is called to auricular fibrillation now as it is one of the commonest forms of fast rates, the ventricular rate sometimes reaching 200 per minute. Complete arrhythmia, differing strength of beat, and pulse deficit distinguish auricular fibrillation from all the other forms of fast rates.

Differentiation.—The polygram and electrocardiogram are both used in studying types of fast rates. In cases other than simple tachycardia and auricular fibrillation clinical examination without the use of the electrocardiogram is not likely to reveal the type of mechanism involved. In the case of auricular flutter observation of the jugular fossa will reveal very rapid pulsations much out of proportion to the rate of the ventricle. Polygrams in such a case may show the rapidly repeated A waves due to auricular contraction. If the ventricular rate is

very fast, say over 130 per minute, polygraph determination is impossible. The electrocardiograph will show the rapidity and sequence of auricle and ventricle perfectly.

Determination of the origin of the contraction impulses in paroxysmal tachycardia is impossible except through the use of the electrocardiograph. Auricular fibrillation shows the characteristic ventricular arrhythmia, the irregularity in strength of beat, and in most cases a pulse deficit, as well as the radial pulse and the ventricular systole. The diagnosis is clinched in the polygraph or in the electrocardiograph.

SLOW RATES

Simple Bradycardia.—There are wide limits to heart rates, and prolonged slow action of the whole heart is not unusual. Rates between 50 and 60 per minute are relatively frequent, and rates between 40 and 50 per minute are sometimes seen where heart affection cannot be proved. However, any rate below 50 is suggestive of heart-block, and any persistent rate below 40 is almost certainly heart-block.

The most common form of slow heart is due to relatively increased function of the vagus nerves. Heart rates varying from 45 to 60 are sometimes seen in individuals convalescing from infectious diseases, typical in the case of typhoid fever convalescence. Other conditions followed by slow rates are jaundice, meningitis, tumor of the brain, and aortic stenosis. Any anatomic condition along the course of the vagus nerves causing pressure on the nerves is apt to produce heart slowing. A slow heart rate may persist for many months, and then gradually increase in rate as the general condition of the patient improves.

Heart-block as a clinical condition in man has been known since 1875. At that time Galabin reported a case of auricular ventricular heart-block with compensation pauses of auricles and ventricles, the ventricles contracting 25 to 30 times a minute. In 1902 Mackenzie described and graphically recorded a disturbance of the heart action which has been provisionally named "sino-auricular" block. In 1910 Eppinger and Stoerk described

a case of sclerosis of the intraventricular septum involving the right branch of the bundle of His, which had manifested itself before postmortem as a clinical case of myocardial degeneration, and with a distinctive electrocardiogram. It is now well known that slowing or complete blocking of the contraction is possible in any conduction area of the heart tissue. By certain experimental means it is possible to produce such effects which will give typical electrocardiograms and other signs.

Sino-auricular Block.—This condition is described under Intermissions below, but attention is called to it here because of its relation to slow heart. The function of the sino-auricular node may become so depressing that alternate contraction impulses fail to materialize, or if they are forming, they fail to reach the auricles. This results in slowing the action of the whole heart to one-half the normal rate.

Auricular-ventricular Block.—The condition known as auricular-ventricular block is due to chronic myocardial changes, specific lesions and accidental anatomic changes or defects of the heart in the region of the bundle of His, or directly affecting the bundle. There may be sclerosis and calcification of the bundle or of the tissue surrounding the bundle. Syphilitic lesions in that area are not very rare. Digitalis, if given in too large doses or administered over too long a period of time, may result in functional auricular-ventricular block.

The effect of these tissue changes by specific lesions is to retard or block the contraction impulses in their passage through the auricular-ventricular bundle to the neighboring muscle tissue. Auricular-ventricular block, therefore, is divided into two stages—partial and complete block. In partial block the first occurrence is a slowing of the contraction impulses, as indicated above. This results in a lengthening of the time interval between auricle and ventricle beyond the time limit, which is 0.22 a second. The delayed conduction becomes more marked, the auricular-ventricular interval becoming longer and longer until an occasional ventricular contraction fails to occur. At this stage of partial auricular-ventricular block intermittency occurs without much change in rate.

The typical slow ventricular rate of auricular-ventricular block is due to the complete blocking of the contraction impulses. Given this situation, the ventricle automatically produces its own contraction impulses in some area of the conduction system below the bundle. The rate and rhythm so instituted are characteristically slow and regular. A complete dissociation of action of auricle and ventricle ensues with both chambers contracting at their own respective rates and not in sequence. The regular slow ventricular rate is below 50 per minute, and may be between 20 and 40 per minute. When auricular-ventricular dissociation occurs the jugular vein may show an extra pulsation between arterial pulses which is due to the contraction of the auricle during ventricular diastole. The polygram will show the ventricular type of tracing with the rhythmic and faster auricular wave (A) occurring. The electrocardiogram reveals the condition perfectly. Both auricular and ventricular complexes are shown to be dissociated, with the P deflection (auricular complex) occurring faster than the Q-R-S-T deflections (the ventricular complex), and sometimes occurring during diastole of the ventricular, and at other times being summated on the various deflection of the ventricular complex.

When complete auricular-ventricular block is due to chronic or specific changes in the tissue of the auricular-ventricular bundle recovery does not occur. If digitalis is the cause of the block, the affection disappears gradually as the use of the drug is stopped.

Differentiation.—In cases of simple bradycardia exercise will cause the pulse-rate to increase gradually. In the case of sino-auricular block, when alternate contractions of the ventricle are dropped out, exercise may result in a sudden doubling of the pulse-rate as the sino-auricular node is stimulated to better function. In the case of complete auricular-ventricular block exercise has very little effect on the rate, and if the work-out is severe, an attack of syncope may occur. The history of occurrence of Stokes-Adams syndrome will also aid in the diagnosis.

Arrhythmias.—"Rhythm" is a word referring to the measurement of time. To describe recurring phenomena as "rhythmic"

is to say that the phenomena repeat themselves at equal intervals of time, and the recurrence may be predicted to fall at certain moments of time.

One of the staunchest characteristics of normal cardiac muscle is rhythmic contraction. Whether the contraction impulses arise in the normal center in the sino-auricular node, or in some other part of the conduction area of the heart, the rhythm of the impulse formation is maintained. This is called the fundamental rhythm of the heart.

Any disturbance of the fundamental rhythm of the heart is termed "an arrhythmia." Any contraction of the heart that results in a break in the rhythm of two heart cycles, without disturbance of the fundamental rhythm, is called "an intermission."

The proper conception of irregular heart action cannot be gained without understanding the relationship of arrhythmia and intermission to fundamental rhythm. Difficulties in diagnosis of irregularities of heart action vary in direct proportion to the ability displayed in differentiating between arrhythmia and intermission. Once the differentiation is made one whole group of possible heart phenomena is eliminated.

The methods of examination to differentiate properly arrhythmia and intermission include palpation of superficial arterial pulsations and ventricular impulses, palpation of arterial pulse while listening to the heart sounds with a stethoscope, and by study of the polygram and the electrocardiogram.

Arrhythmia is the most difficult to determine by palpation in pulses running below 50 per minute and over 120 per minute. The diastolic intervals in a pulse running 140 to the minute may be unequal, but the high rate obscures the sense of rhythm, as does an extremely slow rate. Intermissions of the pulse are much easier to detect by palpation in extreme rates than is arrhythmia. Ten-second counts, repeated many times, will aid in showing up arrhythmia in high pulse-rates. The pulsations may be counted for ten seconds, then after an interval of five seconds another ten-second count made, and so on for several intervals. If the case is one of fast rate, say 120 per minute,

the several counts may be as follows: 20, 18, 17, 22, etc., thus revealing the arrhythmia.

The arteriogram and the electrocardiogram, with their accurate methods of time measurements, will at once reveal disturbances of fundamental rhythm and intermission.

Sinus Arrhythmia.—In this condition the contraction impulses sent into the auricle from the sino-auricular node are slightly arrhythmic. The rate varies with respiratory phases, hastening during the inspiratory phase and slowing during the expiratory phase, and the variation ceases when the breath is held. The condition is not pathologic.

Sinus arrhythmia occurs normally in a great many individuals, but mainly in children. It is often seen in exaggerated form in those individuals who show a marked nervous background, and in cases of fast heart from chronic intoxication, such as in hyperthyroidism. It is also seen in cases of neurocirculatory asthenia.

Unless complicated by premature ventricular contractions, or by short paroxysms of tachycardia, the diagnosis presents no difficulty. If the complications named are suspected the electrocardiogram will clear the diagnosis.

Auricular Fibrillation.—In 1909 Thomas Lewis published a paper entitled *Auricular Fibrillation, A Common Clinical Condition*. In this paper he set forth the real nature of the marked clinical disturbance of the heart previously known as "pulsus irregularis perpetuus," as "delirium cordis," and as "pulsus arrhythmicus." This symptom-complex has been known for many years under any one of the terms just mentioned, but little was known as to the cause or source of the complete ventricular arrhythmia.

Auricular fibrillation is a rather common clinical condition, and generally occurs in hearts that have had, and still have, other signs of disease. The clinical signs are familiar to all observers, and at present they are accurately interpreted by the majority of physicians without recourse to graphic methods of diagnosis.

Auricular fibrillation is generally a terminal condition following years of cardiac affection. It manifests itself in the usual

way of cardiac insufficiency, by dyspnea on exertion, palpitation, cyanosis, edema, and precordial pain. The signs in most cases are: (1) complete ventricular arrhythmia, (2) ventricular contractions of unequal strength value as judged by pulse palpation, (3) a disproportion between the apical impulse and the radial pulse, known as a pulse deficit, and (4) in most cases a ventricular rate exceeding 100 per minute.

The exact condition bringing about this symptom and sign complex is shown by the electrocardiogram to be mainly in the auricle. The auricular muscle-fibers cease to contract rhythmically in response to the contraction impulses which come to them from the sino-auricular node, the pace-maker of the heart. Contractions of individual auricular fibers occur, but each fiber contracts at its own rhythm independently of the other fibers. This results in a momentary contractile movement in one part of the auricle, neutralized by a momentary diastole in other parts of the organ. The net result of this disorder is a distended auricle standing in trembling diastole.

The disturbance in the auricle is due to myocardial degeneration, and to what has been called a "circus impulse." A normal contraction impulse is sent into the auricle by the sino-auricular node. Instead of being conducted in an orderly manner through the walls of the auricle to the auricular-ventricular node (junctional tissue), the impulse is diverted from its normal course by degeneration within the auricular walls, which block the normal impulse paths. The contraction impulses circulate in the auricular walls, being shunted here and there, and in an irregular way are picked up by the auricular-ventricular node, which conveys the impulse to the bundle of His, which passes the impulse on to the ventricles. The result is arrhythmia of the ventricles and generally a fast ventricular rate.

The unequal strength of ventricular contractions depends somewhat upon the rate of the ventricular action. In the course of the arrhythmia it frequently happens that ventricular systoles follow each other very rapidly. The first contraction of the series of rapid contractions will be of normal strength, but the later contractions follow each other so rapidly that there has

been no time for complete recovery of strength from the first strong contraction. Also the short time interval has been insufficient for the proper filling of the ventricles with blood. This situation results in contractions that do not open the aortic valves, thus bringing about a pulse deficit. The pulse deficit must vary with the ventricular rate.

The clinical diagnosis is substantiated in the polygram and the electrocardiogram. In the polygram the arteriogram will show the typical arrhythmia, with ventricular beats of varying strength, while the jugular pulse will show the ventricular type of tracing. The electrocardiogram will show complete arrhythmia of the ventricular complex, with absence of the auricular complex, the P deflection.

Digitalis slows the ventricle, but does not restore normal auricular-ventricular sequence and rhythm except in rare cases. Auricular fibrillation may be paroxysmal, and when it is so, digitalis may terminate the paroxysm. The occurrence of a slow regular ventricular rate in a case of auricular fibrillation that has been freely treated with digitalis is more likely to be due to a complicating auricular-ventricular block brought on by the digitalis than it is to a restoration of normal auricular-ventricular rhythm.

Quinidin sulphate will restore the normal sequence in about 50 per cent. of the cases where it is used.

INTERMISSIONS

The intermittent pulse is commonly mistaken for, or called, an arrhythmia. It is the most usual in occurrence of all disturbances of heart action, and is often the peg upon which is hung a false diagnosis of heart disease.

Premature Contractions.—The majority of all cases of intermittency is caused by premature contractions. Such abnormal contractions depend upon aberrant contraction impulses which arise in an abnormal irritable center located either in the auricle or the ventricle. (The ratio of occurrence of the aberrant impulse in auricle and ventricle is about 1 to 6.) The abnormal impulse usually is formed at some time during the

diastole following a normal ventricular contraction. Therefore the ventricular contraction started by the aberrant impulse takes place before the regular time of its predictable occurrence. It is followed by a compensatory pause, which causes an intermission in the arterial pulse. When the aberrant impulse arises within the walls of the ventricle the compensatory pause is usually exactly two heart cycles; when origin is in the auricle the compensatory pause is a little less than two heart cycles.

The premature ventricular contraction is not normal in strength, the efficiency of its contraction depending upon the time interval between its occurrence and the preceding normal contraction. The ventricle contracting prematurely usually has not had time to recover fully from the last normal contraction before it is forced to contract on an insufficient volume of blood. No surge of blood enters the aorta, and no arterial pulse appears.

Premature contractions of auricular origin show normal auricular-ventricular sequence. Those of ventricular origin do not disturb the rhythm of the auricular contraction, and the normal contraction impulse causing auricular systole falls upon the ventricle during the refractory period, and a ventricular contraction cannot occur at the normal time. When the origin of the aberrant impulse is in the auricular-ventricular node both auricle and ventricle contract simultaneously in nodal rhythm.

Premature contractions are not indicative of heart disease. They occur in individuals who are intemperate, who are overworked, and in those who are underfed. If they recur over a long period of time, especially in patients in middle or old age, or in those showing other signs of heart affection, and when they do not disappear on exercise, myocardial change may be suspected.

Where the premature contraction is ventricular in origin, the polygram will show the presence of a c wave, caused by ventricular systole, occurring somewhere in the abnormally long diastole of the intermission. The electrocardiogram will show a ventricular complex, ventricular in type, occurring

prematurely, and followed by a compensatory pause. The auricular complex, the P deflection, will appear summated somewhere in the ventricular complex, usually near the beginning of the T deflection.

If the premature contraction is auricular in origin, both polygram and electrocardiogram will reveal normal auricular-ventricular sequence in the abnormal contraction, with normal ventricular complexes in the electrocardiogram.

Sino-auricular Block.—This condition has already been described above under the heading of Slow Rate. When a contraction impulse occasionally fails to reach the auricle, through blocking or suppression of function of the sino-auricular node, the auricle and ventricle drop out one complete cycle. The resulting pause of the whole heart is usually a little shorter than two heart cycles, and results in an intermission in the arterial pulse. Both polygram and electrocardiogram will show the pause of the whole heart, lasting nearly two heart cycles.

Auricular-ventricular block has also been described above under the heading of Slow Rate. Dropped beats, causing intermission of the arterial pulse, occur in partial auricular-ventricular block, where the lesion in the bundle of His is not severe enough to produce complete block with dissociation of auricle and ventricle. This cause of intermission is rare.

Partial auricular-ventricular block is marked by a gradual lengthening of the time interval between auricle and ventricle beyond 0.22 second. When this delay in conduction has progressed far enough, a contraction impulse is occasionally lost to the ventricle, and one ventricular systole drops out. The electrocardiogram will show the delay in impulse conduction between auricle and ventricle, and the more or less regular dropping out of every third or fourth ventricular contraction.

Differentiation—The first thing to determine is whether the disturbance is an arrhythmia or an intermittency. The methods to be used have been named above.

If arrhythmia is present the diagnosis lies between two conditions, one being pathologic. Sinus arrhythmia is easily recog-

nized by noting its relationship to the respiratory phases, the constant strength of the ventricular systole, and the absence of pulse deficit. This leaves auricular fibrillation standing alone with its fast ventricular rate, its uneven ventricular power, and its pulse deficit.

To speak of a heart affection as "an arrhythmia" is, in effect, to speak of auricular fibrillation.

If arrhythmia may be ruled out, intermittency remains. Diagnosis usually lies between premature contractions and sino-auricular block. In the case of premature contractions auscultation of the heart will reveal a single or double premature heart sound, occurring coincidently with an intermission of the arterial pulse. If the heart rate be increased through exercise the premature heart sounds and the arterial intermissions will disappear. The polygram and the electrocardiogram will not only show the cause of the intermission, but will locate the origin of the aberrant impulse causing the contraction, as indicated above.

If the mechanism of the intermission be sino-auricular block, auscultation of the heart will reveal the absence of heart sounds during the arterial intermissions. The intermissions are apt to disappear on exercise and increase on holding the breath. The polygram and electrocardiogram are characteristic, as noted above.

Partial auricular-ventricular block at just the stage where every third or fourth ventricular contraction is dropped out is rare in occurrence. This degree of block passes rapidly into complete block with dissociation of auricle and ventricle. The use of the polygram or the electrocardiogram is necessary to make the diagnosis.

ALTERNATION (PULSUS ALTERNANS)

This condition gets its name through the characteristic alternation of strong and weak contraction of the ventricular muscles, resulting in pulses of alternating strength in the arteries. It is of grave import and is of great prognostic value. It occurs in patients suffering from marked myocardial degeneration,

and is sometimes seen in individuals suffering from paroxysmal tachycardia. Alternation is persistent in nature, but may vary in degree. Increasing the rate of the heart, as through exercise, is likely to accentuate the alternations. In the first stages it is likely to occur in the first few pulses following premature ventricular contractions, to pass gradually away until the next abnormal contraction.

The condition is usually discovered through blood-pressure examinations. If the air pressure in the arm bag is increased above the systolic pressure, and then allowed to fall gradually, regular pulse sounds may be heard coming through at a certain pressure that would seem to indicate that the heart was very slow. If the pressure be allowed to decrease a few millimeters of mercury, at a certain pressure the pulse sounds suddenly double in number. Diagnosis by palpation is more difficult, but may be accomplished if all four fingers are laid along the radial artery. The two fingers nearest the heart are then pressed into the artery with sufficient pressure to block the weaker pulsations. This will allow the stronger pulsations to pass through to the other two fingers.

By varying the pressure of the receiving funnel of a recording tambour it is possible to obtain graphic tracings showing alternation. The electrocardiogram will sometimes show the alternation in the amplitude of the deflections of the ventricular complexes.

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PENETRATING ULCERS OF THE STOMACH

DURING the past year the following 7 cases of penetrating ulcer of the stomach were observed by the writer for a long enough period to warrant their being reported. They are presented as they were seen, in an unselected series.

Case I.—Man, fifty-eight, singer, came under observation January 19, 1923.

Past History.—Typhoid at sixteen. Frequent boils up to sixteen years ago. No previous laparotomies. Digestion always excellent. Bowels regular.

Present History.—Seven weeks ago sudden onset of epigastric pain two hours after breakfast. The pain, which traveled horizontally across the upper abdomen, was cramp-like in character and was associated with sub-sternal pressure. Relief followed the next meal, but the pains then recurred regularly about two hours after eating, especially in the evening. Bicarbonate of soda also gave relief, as did belching of sour-tasting gas, but to a lesser degree. On two occasions there was nausea, but no vomiting. The appetite was good, but the patient was afraid to eat. There was some loss of weight and strength.

Physical Examination.—The patient was a cachectic individual of the asthenic habitus. He was found to be 30 pounds (20 per cent.) underweight (normal weight 158 pounds, actual weight 128 pounds). The head and chest were negative. The abdomen was soft. No organs or masses were palpable. There was distinct tenderness in the midepigastrium as well as relief from support of the lower abdomen.

Laboratory Findings.—The fasting stomach contained 9 c.c. of gastric juice, which was congo-positive. There were no food rests. The Ewald test-meal showed free HCl 38, total acidity 54. There was no bile present. The Wassermann test was negative. The hemoglobin was 85 per cent. The urine was concentrated, specific gravity 1025, and contained albumin and indican.

Roentgen Examination.—In the standing position the filled stomach was ptosed 3 inches. The horizontal portion of the lesser curvature was abnormal. In the region near the incisura angularis the lesser curvature showed a plateau-like elevation (Fig. 66). The elevation was 0.5 cm. high by at least 2 cm. long. Between this elevation and the pylorus the lesser curvature was quite flat, showing complete absence of peristaltic waves. On the greater curvature, at a little distance distal to a point exactly opposite the site of the lesion, there were three or four shallow waves or incisures, which were constantly present.

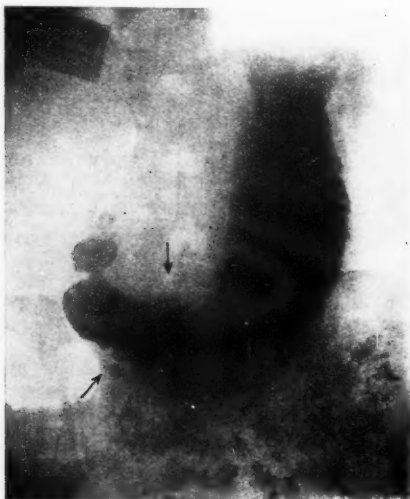


Fig. 66.—Case I. Upper arrow points to niche. Lower arrow points to persistent small waves on greater curvature opposite the lesion. Film taken standing.

In the reclining position the elevation in the lesser curvature was seen to be much more deeply filled out (Fig. 67). It was now 2 cm. deep by 2.7 cm. wide. It was obvious that we were dealing with a very large niche or crater.

The stomach was empty (no retention) at six hours. The duodenum and colon were quite normal.

Clinical Diagnosis.—In view of the age of the patient, the short history, and the previous good digestion, and finally, the large size of the niche, a diagnosis of malignant ulcer was made and the patient was referred for operation.

*Operative Findings.*¹—"Operation was performed February 1, 1923.

¹ By courtesy of Dr. Eugene H. Poole, New York Hospital.

On the lesser curvature of the stomach, about 3 inches from the pylorus, was found a penetrating ulcer about 2 cm. in diameter, boring into the pancreas. The adjacent tissues showed infiltration, but this was apparently inflammatory in nature. The ulcer-bearing portion of the stomach was resected and the duodenal stump inverted and buried. The jejunum was identified 14 inches from the duodenal junction, and this portion of the gut was anastomosed to the cut end of the stomach (Polya operation)."

*Pathologic Report.*¹—"The specimen consists of a resected pyloric end of the stomach 8 cm. in width. It is cut off directly through the pyloric ring. There is a round ulcer 1.5 cm. across, 3 cm. from the pylorus. It is 1.5 cm. deep and has perforated through all the coats of the stomach. The



Fig. 67.—Case I. Appearance reclining.

base consists of dense fibrous tissue and on the outer surface there is a considerable quantity of fat and connective tissue adherent to the base. Microscopic sections present the features of a chronic ulcer."

Course.—The postoperative recovery was quite uncomplicated. Seven months later (September 7, 1923) the patient was re-examined by Dr. Poole. There were no complaints and the man could eat everything. The operative wound was soundly healed. Attempts to reach the patient since then and to re-x-ray him were unfortunately unsuccessful.

Summary.—Recent dyspepsia in a man of cancer age; large niche by Roentgen examination; immediate operation; benign penetrating ulcer, no malignancy; good postoperative recovery.

¹ By courtesy of Dr. William J. Elser, New York Hospital.

Case II.—Widow, fifty, milliner, came under observation October 17, 1923.

Past History.—No serious illnesses. No abdominal operations. Four children, five miscarriages.

Digestive History.—The patient was always constipated, the maximum stool interval being three days. For the past three years she had been taking pills twice a week. The stools were often hard, and contained mucus, but no blood. The patient had had piles.



Fig. 68.—Case II, October 25, 1923.

At the age of fourteen (thirty-six years ago) there was an attack of jaundice which lasted two months.

Twenty years ago the patient began to have severe abdominal cramps, which doubled her up. These pains were most likely to come on after a heavy meal, from immediately to one hour after eating. They were relieved by flaxseed poultices and disappeared for good after a year.

Except for an occasional sensation of abdominal burning the patient remained comfortable to about two and a half years ago, when she began to experience some substernal and epigastric distress after meals. There was regurgitation of food and, for a time, vomiting. Finally, hunger-pains came

on, which were localized in the left side of the abdomen. After a short respite these symptoms recurred and have persisted. Despite the absence of anorexia there has been much loss of weight because the patient was afraid to eat.

Physical Examination.—The patient was a sick-looking woman of the asthenic habitus, much emaciated, and, when first seen, suffering from severe pain. She was 52 pounds (33 per cent.) underweight, her normal weight being 161 pounds and her actual weight 109 pounds. The teeth were missing and the tongue was smooth, clean, and red. The chest was negative. The abdominal wall was thin and there was diastasis of the recti muscles. The liver and the right kidney were ptoed and readily palpable. There was a distinct



Fig. 69.—Case II, October 25, 1923. Large gastric residue at six hours. Niche visualized (arrow).

point of tenderness to the left of the umbilicus. Support of the lower abdomen gave marked relief (the patient had been wearing a self-made supporter).

Laboratory Findings.—The fasting stomach contained 15 c.c. of bile-stained gastric juice positive to congo. Food residues were absent. The Ewald test-meal, removed in forty-five minutes, gave a return of 60 c.c., 60 per cent. of which was solids. Free HCl 47, total acidity 77, mucus increased.

Roentgen Examination.—The stomach was extremely atonic and dilated, and was ptoed 6 inches into the pelvis. At about the middle of the vertical portion of the lesser curvature, arising somewhat from the posterior surface of the stomach, there was a niche 2 cm. deep and 1.5 cm. wide at its base

(Fig. 68). Owing to its posterior origin the crater was most completely revealed when the stomach was but partially filled with the opaque meal. As the stomach filling continued the niche became more and more hidden from view until only its outer portion remained visible. The niche itself was very tender on pressure. Six hours after the barium meal there was a considerable residue in the stomach (delayed gastric emptying). The niche showed up very well, full size, at that time (Fig. 69). At twenty-four hours the stomach was empty.

Clinical Diagnosis.—Severe malnutrition; gastric atony and ptosis; delayed gastric emptying due probably to both atony and spasm; penetrating ulcer of lesser curvature of stomach.



Fig. 70.—Case II, December 5, 1923. Note size of niche with stomach containing one-half of standard barium meal.

Course.—The patient was referred to her physician, Dr. I. A. Lowenthal, who carried out a bed-rest cure, with restricted diet and alkalies, from October 26 to November 26, 1923.

The patient was re-examined December 5, 1923. She reported that while in bed the abdominal pains had entirely disappeared, but since arising (about a week) the pain in the left side had recurred as originally. This pain was explained as being in part due to the drag of the atonic stomach brought on by resuming the upright posture. A tight abdominal binder was recommended. The patient was also told to continue getting as much rest as possible. Objectively, the tenderness in the left abdomen was still present, but was less marked than before. The weight was 107½ pounds, a slight loss on



Fig. 71.—Case II, December 5, 1923. Note size of niche with stomach containing entire barium meal (1 pint).



Fig. 72.—Case II, December 5, 1923. Gastric residue at six hours (compare with Fig. 69). Arrow points to barium in ulcer crater.

the restricted diet. Aspiration of the fasting stomach gave 27 c.c. of green, congo-positive gastric juice without food residue. After an Ewald test-meal (forty-five-minute interval is used in all our work) 100 c.c. were recovered, free HCl 50, total acidity 66. Roentgen examination (second study—Figs. 70, 71) showed that the niche was distinctly smaller, it having contracted down to a narrow channel 1.5 cm. long by 1 cm. wide at its widest (outer) part. There was still a residue in the stomach at six hours (Fig. 72).

On January 18, 1924 the patient reported again for examination. Despite an intercurrent bronchitis she had gained weight to 119½ pounds. For the past two weeks she had been free from her original abdominal pains, her only



Fig. 73.—Case II, January 18, 1924. Niche gone.

complaint in that direction being moderate epigastric distress after meals. The abdominal binder was giving her much relief. Her appetite was improving. Test-meal (third time) showed free HCl 49, total acidity 72, mucus increased. Roentgen examination (third study, fifty-three days after original examination—Fig. 73) showed no evidence of niche, although there was still localized tenderness at the niche level. The stomach residue at six hours was the smallest yet recorded.

Re-examination (March 12, 1924) showed that the patient was completely free from pains, and was enjoying increasing strength and vigor. Objectively, there was no abdominal tenderness. The weight was 125½ pounds, a gain of 18 pounds in five months. Test-meal (fourth examination): free HCl 57, total acidity 77, mucus increased. Roentgen examination (fourth study) showed no niche, gastric tonus somewhat better, ptosis 1 inch less

than at original examination, and only slight gastric residue, which could be readily explained by the degree of ptosis and atony still present (Fig. 74).

Summary.—Old history of dyspepsia in a woman of fifty; marked emaciation; advanced gastric atony and ptosis; penetrating ulcer of lesser curvature



Fig. 74.—Case II, March 12, 1924. Stomach almost empty at six hours (compare with Figs. 70, 72).

of the stomach; delayed gastric emptying; disappearance of niche, relief of symptoms, and almost complete cure of delayed gastric emptying after bed-rest and routine medical treatment.

Case III.—Butcher, fifty-nine, married, came under observation November 7, 1923.

Past History.—Typhoid fever at eight years of age. No other serious illness. No operations.

Digestive History.—Always well except for constipation during the past two years. One month ago onset of pains deep in the chest, radiating from the epigastrium to the back. The pains would come on two hours after meals, except after breakfast, and would last for two hours. They would be relieved by a hot-water bag or by a hot bath; there was no immediate relief from lying down. The patient had stopped work two weeks ago on account of these symptoms. There was no dysphagia and the appetite remained good. There was a loss of about 10 pounds in weight. The best previous weight was 120 pounds in 1920. Recently there had been some difficulty in urination.

Physical Examination.—Asthenic, emaciated, somewhat cachectic man.

Malnutrition of 41 pounds, the actual weight being 108 pounds, and the normal calculated weight for height and age 149 pounds. The teeth were all missing. There was no abdominal tenderness, but there was relief from support of the lower abdomen. The prostate was enlarged.

Laboratory Data.—Hemoglobin 100 per cent. (Sahli). The fasting stomach contained 5 c.c. of congo-positive gastric juice, no food residue. Ewald test-meal: free HCl 43, total acidity 70, mucus plus. Urine: specific gravity 1015, hyaline casts, no albumin.

Roentgen Examination.—Stomach was ptosed and moderately atonic. On the lesser curvature near the incisura angularis there was a niche, 1 cm.



Fig. 75.—Case III, November 8, 1923. Appearance of niche standing.

deep by 1 cm. wide (Figs. 75, 76). Unfortunately no note as to local tenderness was made at the time of examination. There was no gastric residue at six hours. The duodenum was normal.

Clinical Diagnosis.—Penetrating ulcer of lesser curvature of the stomach.

Course.—The patient was referred to his physician, Dr. N. S. Rawdin, who carried out a bed-rest cure with restricted diet and alkalis from November 10 to December 6, 1923.

Re-examination (December 7, 1923): Pain in chest gone. The only complaint was a disagreeable sensation of burning in the abdomen. The bowels were occasionally constipated. Physical examination of the abdomen



Fig. 76.—Case III, November 8, 1923. Appearance of niche reclining.



Fig. 77.—Case III, December 7, 1923. Note diminution in size of niche.
Film standing.

was again negative. There had been a gain in weight of 3 pounds, the weight now being 111½ pounds. Test-meal showed free HCl 16, total acidity 42, mucus increased. Roentgen examination showed that the niche had contracted down greatly, its diameter being but 3 mm. in both directions (Fig. 77). The patient was now put on convalescent ulcer management—bland diet and alkalies.

Re-examination was made on January 15, 1924. The abdominal warmth sensation was now only occasional and mild in degree. The bowels were still somewhat costive. The weight was now 121 pounds, representing a gain of 13 pounds in nine weeks. The test-meal (third examination) showed free HCl 23, total acidity 55, mucus increased. Roentgen examination



Fig. 78.—Case III, January 15, 1924. Niche gone. Film standing.

(third study) showed absolutely smooth contour of lesser curvature in region of old niche (Fig. 78). The patient was anxious to go back to his work.

Report from Dr. Rawdin (March 16, 1924): The patient is now working. He is free from symptoms and has further gained weight to about 130 pounds.

Summary.—Recent history (one month) of hunger-pain in man of cancer age; ulcer niche of lesser curvature; disappearance of niche with disappearance of symptoms and rapid gain in weight to new high level after bed-rest cure and routine medical management.

Case IV.—Truckman, forty-three, married, came under observation October 4, 1923.

Past History.—No serious diseases or operations. The patient has been constipated for the past ten years. His bowels move, on the average, every second day, and he takes a cathartic about once a week. The meals are always irregular and hurried on account of his work. For some years he has had fulness, distention, and belching for about an hour after meals, but no acute distress. There has been no vomiting. The appetite has always been good.

Present History.—One month ago sudden onset of severe epigastric pain one hour after eating. The pain radiated to the back and up along the spine to the neck, was associated with nausea, and was relieved after fifteen minutes by vomiting. After this attack the pain recurred twice daily one hour after meals, and occasionally at night. Vomiting was rarely repeated, but there was considerable belching. The pain was relieved by milk and cream. The constipation required catharsis. The appetite remained good. The weight had dropped from about 142 to 133 pounds.

Physical Examination.—Sthenic habitus. Abdomen tender in epigastrium, otherwise negative. Actual weight 133 pounds; normal weight for height 144 pounds.

Roentgen Examination (at Vanderbilt Clinic, October 17, 1923).—The stomach was moderately ptosed and atonic. On the lesser curvature about 4 cm. from the cardia there was a niche 5 mm. deep by 5 mm. wide. No observation was made as to local tenderness.

Diagnosis.—Penetrating ulcer of the stomach.

Course.—On October 20th the patient was put on the routine ambulatory treatment for gastric ulcer practised at the Vanderbilt Clinic, consisting of a fairly liberal bland diet and alkalies after meals. By that time the weight had further diminished to 129 pounds. Finding that the pains persisted despite the above management, the patient restricted himself to a regimen of cream and milk, later adding chicken. Meat and soup, however, would cause a recurrence of pain. By December 17th the patient had gained weight to 132½ pounds and his pains had practically disappeared. Re-examination on December 19th (two months after the first Roentgen study) showed that the original niche had disappeared entirely. There was, however, some question whether a new small niche, not more than 1 mm. deep, had not developed low on the lesser curvature almost at the incisura angularis. The films, unfortunately, were not clear as to this point. In order to study the patient more carefully he was referred to the Montefiore Hospital, where, however, he was not admitted until February 3, 1924. By this time he was practically symptom free, but was quite willing to go through with a bed-rest Sippy cure for one month in order to avoid, as much as possible, recurrence of his trouble. On February 4, 1924 the fasting stomach contents contained 20 c.c. pure gastric juice, free HCl 52, total acidity 78. The Ewald test-meal, removed in forty-five minutes, gave a return of 64 c.c., 25 per cent. of this being solids, free HCl 63, total acid 92. Roentgen examination February 12th again showed a suspicion of a minute niche near the incisura, but this could not be recorded with certainty. Another (fourth) x-ray a week later (February 19th) showed no evidence of niche. The patient did very well on the bed-rest cure, lost all his symptoms, and gained 11 pounds, practically reach-

ing his normal weight by the time of discharge (March 4, 1924). He was seen again three weeks later and found to be quite well.

Summary.—Short history in a man of forty-three; distinct ulcer niche near cardia; disappearance of this niche and almost complete relief of symptoms after ambulatory treatment of two months' duration; possible development of a small new niche at another point; complete relief of symptoms and no trace of niche anywhere in stomach after one month's bed-rest Sippy treatment.

Case V.¹—Woman, thirty-four, married, came under observation August 27, 1923.



Fig. 79.—Case V, August 28, 1923.

History.—Abdominal pain and discomfort for nine months. For the past two months the symptoms had been worse. The pain, which was located in the epigastrium, came on one hour after meals, reaching its maximum an hour later. It was most marked after supper and more especially after eating soup. There was considerable fullness and bloating, relieved by belching, but this was difficult and infrequent. The distress was also relieved by vomiting of sour food once or twice a week. There was no heartburn. The appetite was poor and the bowels were constipated.

Physical Examination.—Abdomen negative. Weight 101 pounds.

Röntgen Examination (August 28, 1923).—At about the middle of the lesser curvature of the stomach there was a niche 5 mm. deep by 8 mm. wide at its base (Fig. 79). There was no gastric retention six hours after the barium meal.

¹ By courtesy of Dr. Marks S. Shaine, Vanderbilt Clinic.

Course.—The patient was admitted to a hospital, where a bed-rest cure with restricted diet and alkalis was carried out for two weeks (from September



Fig. 80.—Case V, December 12, 1923. Practically no change in size of niche three and a half months later.



Fig. 81.—Case V, February 20, 1924. Niche gone six months later.

13 to 27, 1923). On discharge the patient was free from symptoms. She then weighed 98½ pounds.

Re-examination October 19, 1923: No symptoms. Weight 105 pounds.

Re-examination November 10, 1923: No symptoms. Weight 107 pounds.

Re-examination December 12, 1923: No symptoms. Weight 109 pounds. Roentgen examination (second study) showed niche about the same in size as before (Fig. 80).

Re-examination February 12, 1924: No symptoms. Weight 109½ pounds.

Re-examination February 20, 1924: No symptoms. Roentgen examination (third study) shows no evidence of niche (Fig. 81).

Summary.—Short history in a young woman of thirty-four; niche of lesser curvature; relief of symptoms after two weeks' bed-rest cure; persistence of niche for from four to six months after original examination. (Query: Would niche have healed faster if bed-rest had been longer?)

Case VI.—Man, forty-four, married; operator on dresses; came under observation December 11, 1923.



Fig. 82.—Case VI, December 11, 1923. Niche near cardia. Film reclining.

Past History.—Negative.

Digestive History.—Except for being constipated all his life and for an operation for piles four years ago he had been quite well until six months ago. At that time there was gradual onset of substernal pressure and globus. The swallowing, however, was normal and there was no vomiting or regurgitation.

Three months ago the patient began to have real pain, coming on three hours after eating, located at the midsternum, and radiating through to the back. There was no pain in the abdomen. As time went on the pains started earlier, about one hour after meals, and lasted longer. Although food relieved

the pain, phagophobia was so decided that the patient lost 25 pounds in weight in six months.

Physical Examination.—The patient was a white-haired, emaciated man of sthenic habitus, 34 pounds underweight, his actual weight being 124 pounds and his normal weight 158 pounds. Many teeth were missing, the rest were in poor condition. The abdomen was not tender on pressure. There was relief from support of the lower abdomen.

Laboratory Tests.—The fasting stomach contained 30 c.c. of gastric juice in which the free HCl was 50 degrees, and the total acidity 66 degrees. There was no food residue. Forty-five minutes after the standard Ewald test-



Fig. 83.—Case VI, December 11, 1923. Gastric residue at six hours. Niche not visualized.

breakfast 190 c.c. were recovered, 60 per cent. solids, free HCl 34, total acidity 59, mucus increased. The urine was negative except for high specific gravity (1030).

Roentgen Examination.—The stomach was ptosed and atonic. High on the lesser curvature, just beneath the cardia, was a rather large niche, 1 cm. deep by 1.5 cm. wide (Fig. 82). This was very tender on pressure. The rest of the stomach outlines were normal in contour, there being no evidence of incisura or hour-glass contracture. At six hours there was a considerable residue in the stomach (Fig. 83), but at twenty-four hours the stomach was empty.

Clinical Diagnosis.—Penetrating ulcer of the lesser curvature near the cardia.

Course.—The patient was restless and was not easily managed. Several attempts at bed-rest cure by the writer and others proved abortive after two to four or five days despite the fact that the symptoms disappeared almost entirely within the first thirty-six to forty-eight hours. Without our knowledge the patient consulted a surgeon and underwent operation.

*Operative Findings.*¹—"Operation took place January 17, 1924. A penetrating ulcer, about $\frac{1}{2}$ inch deep and admitting the small finger, was



Fig. 84.—Case VI, March 2, 1924. Note increased size of niche at cardia (arrow) and hour-glass contracture of stomach. Film standing.

found on the lesser curvature not far from the cardia. There was considerable induration in the neighborhood. A V-shaped excision was done without gastro-enterostomy. A couple of inflamed glands were removed. Pathologic examination of the excised tissue by Dr. William C. Thro showed no evidence of malignancy."

Postoperative Course.—The patient made a good recovery from the intervention. He left the hospital February 10, 1924, weighing 106 pounds. The patient was re-examined by the writer on February 27th. The original

¹ By courtesy of Dr. Benjamin T. Tilton, St. Mark's Hospital.

hunger-pains in the chest were gone. The patient now complained of heart-burn, of some pain in the back which was constant, and of constipation. He had vomited four times in the past week, one or two hours after eating. His weight had gone up to 115½ pounds. The abdomen was tender at the scar, but was otherwise negative.

Re-examination took place March 2, 1924. The patient had not vomited again and was feeling better. His appetite, however, was still poor and the pain in the back, though less severe, was still present. For the past two days he had had hiccups. His weight was now 116½ pounds. The fasting stomach contained 20 c.c. of food residue which was positive to congo. After the test-meal 80 c.c. were recovered, 50 per cent. solids, free HCl 26, total acidity



Fig. 85.—Case VI, March 2, 1924. Appearance reclining.

44. Roentgen examination revealed a hypertonic hour-glass stomach (Figs. 84, 85). The hour-glass incisure was at the lower part of the pars media, with a narrow channel of communication between the two gastric pockets along the lesser curvature. Higher up on the lesser curvature and corresponding exactly to the position of the original niche was a larger niche 2.5 cm. deep by 1.5 cm. wide (Figs. 84, 85). Six hours after the barium meal the stomach contained a much larger residue than at the original examination (Fig. 86).

On March 25th the patient reported that he had gone to the country to convalesce more rapidly. His symptoms still annoyed him and he felt unable to get back to his work.

Summary.—Short history in a man of forty-four; niche on lesser curva-

ture near cardia; delayed gastric emptying; penetrating ulcer, corresponding to niche, excised at operation; development of larger niche in original posi-



Fig. 86.—Case VI, March 2, 1924. Gastric residue at six hours (compare with Fig. 83). Niche not visualized.

tion and of hour-glass contracture lower down following operation; increase in gastric stasis after operation.

Case VII.—During the period in which the preceding cases were observed we saw at the Vanderbilt Clinic a man who, on x-ray examination, showed a typical ulcer niche on the lesser curvature of the stomach. This patient left the clinic and accepted the advice of a doctor who recommended surgical intervention. The operation was performed by a very competent

surgeon, the ulcer was found and excised, and an anastomosis made (Billroth II). About eight days later the patient died, postoperative pneumonia being assigned as the cause of death.

DISCUSSION

History and Clinical Picture.—Even so short a series of cases as the present offers several points of interest. First, perhaps, is the age of the patients. With one exception these were all people fairly well along in years, viz., fifty-eight, fifty, fifty-nine, forty-three, thirty-four, forty-four—the average age being forty-eight. This period of life is commonly associated in our minds with cancer rather than ulcer. Yet the evidence seems to be more and more definite that ulcer is not so much a disease of youth as is commonly thought to be the case. Thus Smithies has recently pointed out that barely 9 per cent. of ulcer suspects under thirty-one years of age actually have gastric or duodenal lesions.

Another point in this connection is the rather unexpected shortness of the history obtained in the above cases of penetrating ulcer. Five of our 6 cases had practically no indigestion prior to six months before coming under observation. This feature also we have been wont to associate with cancer rather than with ulcer. If to all this is added the cachectic appearance of 2 of our patients, it is easy to see how a clinical diagnosis of cancer can be made in many cases of penetrating ulcer of the stomach.

Still another item of interest is the location of the pain. This was most commonly present in the chest and back, and seemed to correspond in a general way with the location on the lesser curvature—the higher up the lesion, the higher the pain. Striking was the frequent absence of pain in the abdomen. However, in one case (Case II), where there was marked ptosis, the pain was felt distinctly in the left side of the abdomen. As is the rule in all organic lesions, the pain was real, and was not a mere distress or discomfort.

Judging from our experience it seemed easy to overlook localized abdominal tenderness on routine physical examination.

We are not now referring to epigastric plexus tenderness which is so common in all sorts of digestive disorders. After the niche was localized by x-ray, however, it was found to be very sharply tender on pressure. This tenderness became progressively less marked, as the lesion healed under observation.

Roentgen Diagnosis.—In large niches the Roentgen diagnosis is relatively simple. When the niche is small, however, and particularly in cases where the ulcer does not spring squarely from the lesser curvature, difficulties may arise in interpretation. In such instances it is important to observe the stomach in the process of filling in order to catch sight of the niche before the completely distended organ hides it from view (Figs. 70, 71).

Conversely, there may be difficulty in the proper interpretation of other shadows that may resemble niches. Perhaps the most common source of trouble is the duodenojejunal flexure, which may appear partly visualized above the incisura angularis as though springing from the lesser curvature of the stomach. This difficulty may generally be overcome by comparing the findings in the reclining with those in the standing posture. Since the small intestine is fixed at that point, whereas the stomach is free, the shadows in question will probably not appear in the same relation to each other in both positions. Other rarer sources of error, such as jejunal diverticula and stone shadows, have been pointed out by Cole.

It has been claimed that a large niche is likely to be malignant in nature, and the impression has gained ground that size alone should decide one's procedure. Thus Carman says: "When the niche representing the crater is 2.5 cm. or more in diameter, cancer is usually found in the ulcer on microscopic examination. Unfortunately, a smaller ulcer may also be carcinomatous, or a larger one may exceptionally be benign." It was because of such dicta as this that we advised immediate operation in our first case (Figs. 66, 67). Such, however, would not be our procedure in the future. We are now so convinced of the inherent tendency of benign ulcers to heal that we would not hesitate to try the effect of a bed-rest cure in every case of niche no matter how large the crater. Only if there seemed no indication of

diminution in size after a most thorough treatment would we incline to the diagnosis of cancer.

Treatment.—In our opinion the treatment of penetrating ulcers of the stomach should consist of careful medical management. Despite the fact that a niche may ultimately disappear following a very short rest period (two weeks), as in Case V, or even after ambulatory treatment alone, as in Case IV, we feel that a properly conducted medical cure calls for uninterrupted rest in bed for four weeks at the least. Oehnell, who has reported by far the largest number of good results from medical treatment, kept his patients in bed for five to six weeks, and attributes the poor results in certain cases to too short a period of absolute quiet.

We do not favor the routine surgical treatment of penetrating gastric ulcers for the following reasons:

1. The results of our own (admittedly limited) experience. Of our 7 cases, 3 were operated on by excellent surgeons. Two cases survived operation. In only one was the result satisfactory. On the other hand, in all 4 cases treated medically, and by no means ideally at that, the niche disappeared and the patients are so far well (five, four, five, and seven months later, respectively).

2. The combined results of others who have tried medical treatment. The classic work of Oehnell has already been referred to. He secured complete disappearance of the niche in 31 out of 34 cases, and a diminution in size in the remaining 3. Other observers who have reported disappearance of the niche after medical treatment are, in the order of their publications: Hamburger (3 cases), White (2 cases), Buckstein (1 case), Sippy (number not stated), Shattuck (5 cases), Diamond (14 cases), Einhorn (5 cases), Caillé and Moutrier (6 cases), Timbal (1 case), Feissly (2 cases). Thus there have been reported since 1918 a total of 73 cases (not counting our own) in which the niche disappeared or diminished in size following medical treatment.

3. The results of recent pathologic studies which emphasize the spontaneous tendency of peptic ulcers to heal. The time

was not so far distant when it was thought by many that a so-called "chronic ulcer" of the stomach would not heal unless surgically interfered with. The infrequency of healed lesions as seen postmortem was pointed to as corroborative proof of the soundness of this notion. It now seems probable that the reason pathologists did not find healed ulcers more frequently in the past is not because the ulcers did not heal, but because they often healed so well that more than a superficial inspection was necessary to reveal evidence of their former existence. According to Holzweissig (who found gastric or duodenal ulcers or scars in 6 per cent. of a series of 1759 routine autopsies), the characteristic finding in the healing of a peptic ulcer is a defect in the continuity of the muscularis mucosæ. All other coats, including the epithelium, may be so completely restored as to give a superficially normal appearance to the former ulcer-bearing area.

4. The increasing evidence that some individuals may have a "predisposition" to ulcer—so-called diathesis. In such subjects there may be repeated cycles or crops when the same or different ulcers may heal, break down, and heal anew. Patients with ulcer niches that disappeared and then recurred either at the same site or at new locations have been observed by Oehnell and by Jacobaeus and probably by others as well. The possibility of this phenomenon having occurred in Case IV of the present series has already been mentioned. It is obvious that an ulcer diathesis, if such really exists, cannot be affected by either medical or surgical treatment as it is now practised.

SUMMARY AND CONCLUSIONS

1. Seven cases of penetrating ulcer niche were observed during the past year.

2. Penetrating ulcers may clinically and roentgenologically resemble cancers. A differentiation between the two may be made by observing the effect of bed-rest on the size of the niche.

3. All the cases of the present series that were treated conservatively showed disappearance of the niche and became well. It is not implied that they will remain well.

4. Of the 3 cases operated on, 1 became well, 1 is still an invalid, and 1 died following the intervention.

5. Medical treatment is the method of choice. A properly managed cure implies absolute rest in bed for from one month to six weeks.

6. No form of treatment yet devised seems to affect the tendency to recurrence which is presumably due to some unknown "constitutional" factor or "diathesis."

Note on Revision of Proof.—Case III was re-examined on April 19, 1924 on account of recurrence of symptoms of three weeks' duration. The niche was found to have returned at the same site as originally, the dimensions being 7 by 12 mm.

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CLINIC OF DR. JOHN WYCKOFF

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AURICULAR FLUTTER WITH 2 TO 1 BLOCK AS SEEN IN ORGANIC HEART DISEASE

THIS not infrequent change in the pathologic physiology of heart disease will be discussed today for the following reasons:

1. Auricular flutter is frequently unsuspected by physicians of considerable experience.
2. If correctly diagnosed auricular flutter in the great majority of cases responds to treatment, and often with a dramatic improvement of the patient's condition.

Briefly, auricular flutter is a condition in which the auricles beat at a rapid rate, usually between 200 and 330 times a minute (most frequently between 260 and 320). This extremely rapid rate is due to a stimulus which does not arise in the sino-auricular node, but to one which travels in a cycle around the openings of the superior and inferior vena cava into the right auricle. When such an impulse travels at a rate of 300 or under, each complete circuit is followed by an auricular contraction. This rapidly contracting auricle bombards the a-v. bundle with an impulse each time it contracts. The bundle rarely can transmit such a tremendous number of impulses, and in most cases every other impulse fails to cross the bundle or is blocked. This is known as 2 to 1 block, and when it occurs we have a ventricular rate which is just half as fast as the auricular rate. The most frequent ventricular rates in auricular flutter are between 130 and 160 per minute. In some cases the bundle will

not transmit every other beat, and then we may have a block of higher grade, the ventricles responding to only every third or fourth auricular beat. In other cases there is no regularity in the transmission of impulses, the a-v. bundle in these cases blocking at various times two or three impulses before allowing one to cross to the ventricle; this results in an irregular ventricular rhythm, but Alfred Cohen says: "Even if apparently irregular, a dominant order underlies them, in that the cycles or groups of cycles are multiples of a greatest common divisor."

In auricular flutter with a-v. block of greater degree than 2 to 1 the ventricular rate is not accelerated sufficiently to be, of itself, a factor in producing heart failure. Such cases are not, in our experience, met with as frequently, so we are confining ourselves to the discussion of auricular flutter occurring with 2 to 1 block. For short periods of time in certain cases of auricular flutter the bundle will transmit all the auricular impulses. This is, of course, followed by a tremendously rapid ventricular rate, and if maintained for any time, is usually accompanied by syncope.

Auricular flutter may be paroxysmal or chronic. Patients having the chronic type frequently give a history of preceding attacks of the paroxysmal flutter. Auricular flutter is observed most frequently in arteriosclerotic heart disease, although it does occur in other types of organic heart disease. It is also seen in acute infections, notably in pneumonia and influenza. In the infections the condition is masked by the infection and is frequently unrecognized.

The types of flutter that we are discussing today are those in which the symptoms are to a great measure due entirely to the rapid rate; cases in which, when the flutter is removed, the patient's symptoms rapidly disappear. As this type of flutter occurs usually in patients whose hearts are the seat of organic disease, eliminating the flutter does not necessarily give them a normal cardiac reserve, nor do they live indefinitely, but frequently, if not usually, the most serious symptoms disappear and the patients are greatly improved.

During the past two years we have admitted to the service

of the Third (New York University) Medical Division, Bellevue Hospital, 420 cases of patients with organic heart disease with heart failure; of this number 7, or 1.6 per cent., had auricular flutter with 2 to 1 block.

Sir James McKenzie makes the statement, in speaking of auricular flutter, "This rare condition is difficult to recognize without graphic or other instrumental methods of investigation." The term "rare" is, of course, a relative one, but it is a condition which every busy practitioner is apt to meet in his routine practice. Of the cases of flutter which we are today describing all were diagnosed clinically before the diagnosis was proved by the electrocardiograph except one; I think that the average case of auricular flutter occurring with 2 to 1 block can nearly always be diagnosed without instrumental aid by one who is cognizant with the methods of making the diagnosis.

Patients with auricular flutter generally give a history of previous attacks of palpitation, associated with substernal distress or actual pain. During such attacks pulmonary symptoms are prominent. Our 7 cases were admitted with the following diagnoses, made by the admitting physician, or by outside physician: 1 pulmonary edema, 3 pneumonia, 1 bronchial asthma, 1 chronic pulmonary tuberculosis, and 1 chronic cardiovalvular disease, with heart failure; 6 of the 7 cases being admitted with pulmonary diagnoses.

The ventricular rate is usually between 130 and 165. The rhythm is regular. The sounds are generally distinct unless they are marked by adventitious pulmonary sounds. I have never heard gallop rhythm in a case of flutter. Although the dominant rhythm is regular, it may be occasionally interrupted by a premature contraction or a slight irregularity, due to a slight change in the a-v. conduction time; however, these irregularities are only incidental and do not detract from the fact that the heart is usually beating absolutely regularly. The rate is little influenced by rest, exercise, or excitement. In chronic cases the ventricle will beat for weeks with a

variation of less than 10 to the minute. A chart kept of the ventricular rate is a great practical help in diagnosing these cases. Vagal pressure (applied by firm pressure on the carotid sheath) will slow the ventricular rate (see Figs. 90-92), sometimes giving a complete ventricular standstill for several seconds; slight syncope may occur during this standstill, but the rhythm will reassert itself as soon as the pressure is relieved. The pulse is variable; there is frequently pulsus alternans present. When this is marked only every other beat will reach the radials (see Fig. 87), at other times only a few beats will fail to reach the wrist (see Fig. 87), and sometimes they all come through regularly. It is always small, but may be of quite high tension. The pulse chart is frequently misleading, and many cases of flutter are missed in hospital practice because the pulse chart is watched instead of the actual ventricular rate.

Auricular pulsations in the neck are sometimes seen and, when present, are absolutely diagnostic. Contrary to what might be expected, they are hard to see if the jugulars are dilated and there is an incompetency of the tricuspid valve. When such a condition is present the ventricular type of jugular pulse seems to obliterate all auricular pulse waves. When the jugulars are not dilated, or only slightly dilated, a wave may be observed at the jugular cistern, which can be seen to beat twice each time the ventricle beats once if the heart be auscultated and the jugular cistern inspected simultaneously. This was demonstrated to students in two of our cases.

The following 2 typical cases of flutter are described in some detail. The diagnosis of flutter with 2 to 1 block was made clinically in the 7 cases of our series except the first one, and in 4 of the cases it was made by interns on duty in the wards, showing rather conclusively that the clinical diagnosis is not only not impossible, but fairly simple. Each case was proved to be flutter by graphic methods, and the electrocardiographs and charts of these 2 typical cases showing the patients' course and reaction to treatment are also shown.

Case I.—J. K., occupation janitor, white male, aged sixty-nine years, born in the United States, admitted to Ward A6 Bellevue Hospital April 5, 1922. Chief complaint: Dyspnea.

Family History.—No bearing on the case.

Previous History.—Has taken 2 or 3 glasses of beer a day all his life; drinks 2 cups of coffee and 1 of tea every day; smokes 2 or 3 cigars a day. He remembers none of the diseases of childhood. Gonorrhea forty-eight years ago, and a chancre thirty-nine years ago; was told at that time he had syphilis, and was treated with mercury and potassium iodid for two years. One year ago he was told that his blood was still 1+. Twelve years ago he sustained a fracture of three ribs, which was followed by an attack of pneumonia, from which he made an uneventful recovery. His greatest weight was 250 pounds two months before admission.

Present History.—For the past two years patient has noticed that he was growing more short of breath upon exertion; during the past two months this has grown worse, and he has noticed that his feet were swelling. He has been sleeping well, however, and was able to sleep lying down. He has had occasional attacks of palpitation during the past two years. He said that suddenly his heart would begin to beat very fast, and that with the palpitation he experienced a feeling of substernal pain; this pain did not radiate. He went to bed as usual last night at 9 o'clock. He went to sleep almost immediately. About 1 o'clock this morning he woke coughing and spitting frothy mucus; he was very short of breath and thought he was going to die; he also had the substernal pain as described above. His condition was so serious that his family at once ordered an ambulance and he was brought to the hospital.

Admission Note.—Dyspneic, orthopneic, coughing blood-streaked mucus; jugulars dilated and pulsating; liver palpable 12 cm. below ensiform, pulsating; sclerosis of radials, brachials, and temporal arteries; pulse at times difficult to get and irregular, rate 100; ventricular sounds regular, rate 148; impossible to localize the apex-beat, A2 louder than P2. A systolic murmur is heard with maximum intensity at the apex transmitted to the left. Small and large moist râles are heard all over the lungs. Blood-pressure: systolic 150, diastolic 100. Provisional diagnosis: Heart failure of the congestive type, pulmonary edema. The patient was given atropin, gr. 1/100; epinephrin, 10 minims of a 1:1000 solution, and Majendie solution, 7 minims, all by hypodermic. He became much more comfortable and slept.

He was seen by me the next day, April 6, 1922, at 10 A. M., when the following note was made: A stout man, dyspneic and orthopneic; veins of neck dilated and pulsating; liver palpable $13\frac{1}{2}$ cm. below the ensiform and pulsating. There is edema of both lower extremities, and signs of congestion at the bases of both lungs. Despite these marked symptoms of heart failure, the patient seems fairly comfortable, and says he slept a considerable part of last night. The apex of the heart could not be localized. Cardiac dulness extended to the right 4 cm. in the fifth space, and 15 cm. to the left in the sixth space; A2 is louder than P2. There is a distinct blowing systolic murmur heard with maximum of intensity in the sixth space, 15 cm. to the left of the median line, and transmitted into the left axilla. The ventricular rhythm

is regular, rate 142 per minute, the pulse at times showed a marked alternans. Blood-pressure, 148/85.

Diagnosis.—Arteriosclerotic heart disease (possibly luetic); enlarged heart; ectopic tachycardia; Class III (heart failure at rest). An electrocardiogram was ordered, which showed that the patient had auricular flutter

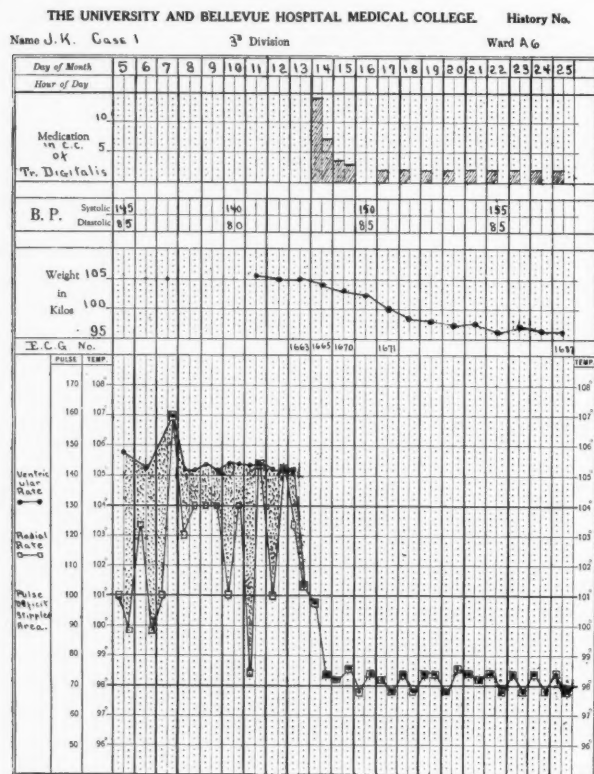


Fig. 87.—Graphic chart of Case 1, showing ventricular and radial rates, pulse deficit, weight, and digitalis medication. Pulse deficit due to pulsus alternans.

with 2 to 1 a-v. block and intraventricular block. As the patient's condition was improved, it was decided to withhold digitalis, and see if normal rhythm would reassert itself. For this reason he was kept at rest in bed on a back-rest, on a simple diet, with fluids limited to 1500 c.c. until April 13th (eight days after admission). During this time the following laboratory examina-

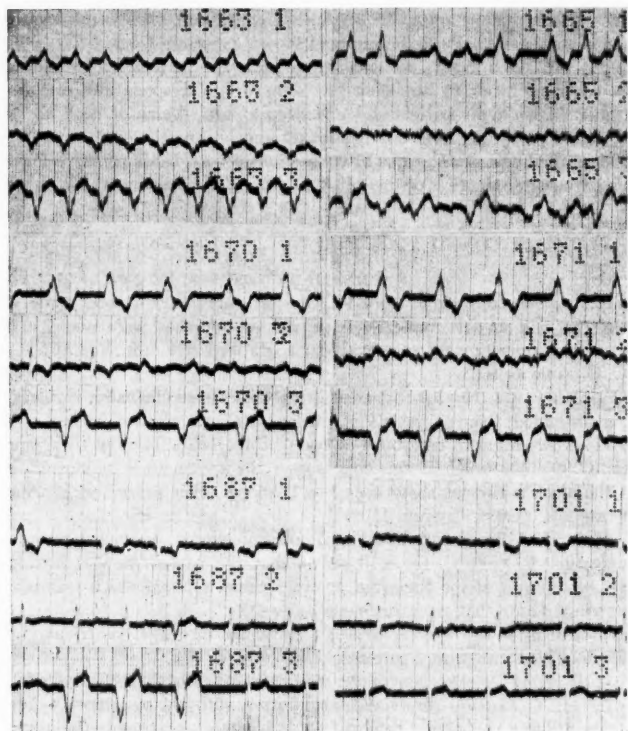


Fig. 88.—Electrocardiograms from Case I:

1663, Auricular flutter 2 to 1 a-v. block. Intraventricular block. Auricular rate 276, ventricular rate 138. Electrocardiograms similar to this were obtained daily from April 5th to April 13th inclusive.

1665, Auricular flutter, varying a-v. block. Intraventricular block. Auricular rate 286, ventricular varies about 110.

1670, Auricular flutter 4 to 1 and 3 to 1 a-v. block. Varying intraventricular block. Auricular rate 296, ventricular rate varies between 74 and 98.

1671, Auricular flutter 4 to 1 a-v. block. Intraventricular block. Auricular rate 322, ventricular rate 80.

1687, Auricular fibrillation. Varying intraventricular block. Ventricular rate 74.

1701, Auricular fibrillation. Ventricular rate 74.

tions were made. Urine: amber, specific gravity 1014, acid, albumin 2 plus, no sugar, a few hyaline and granular casts. Red test: 10 per cent. in two

hours. Wassermann: negative to both alcohol and cholesterol antigens. Blood chemistry: N. P. N. 35 mg. per 100 c.c., creatinin 1.6 mg. Per 100 c.c.

On April 13th it was decided to digitalize the patient. The following note was made prior to his being given the drug: dyspnea and orthopnea continue. Last night patient did not sleep at all. Veins of neck are still dilated and pulsating, liver is pulsating $11\frac{1}{2}$ cm. below the ensiform. There is still marked edema and signs of congestion of both bases persist. Patient received hospital tincture of digitalis as follows (Eggleston method):

11 A. M.,	13.5 c.c.
5 P. M.,	7 c.c.
12 Midnight,	3.5 c.c.
6 A. M.,	3 c.c.

During the afternoon of April 14th frequent observations were made, and though he said he felt clinically improved, no changes were noted in his heart rate or rhythm. He was electrocardiographed at 1 A. M., and at 5 P. M., E. C. G. same as 1663.

April 14, 1922, 10 A. M.: Patient greatly improved clinically, jugulars no longer distended; liver palpable 9 cm. below ensiform; ventricular and pulse-rate 114; there seem to be groups of two or three beats followed by a pause. An E. C. G. 1665 taken at this time shows the continuance of flutter, but that the block is varying sometimes 2 to 1, and at other times 3 to 1. Auricular rate 284, ventricular rate 110.

April 15, 1922: Heart usually completely regular, ventricular rate by auscultation, 72. E. C. G. 1670 shows that the patient now is having a 4 to 1 block most of the time, but at other times a 3 to 1 block. It is also interesting to note that after the longer pauses the Q. R. S. is normal, but that it is bizarre after the shorter pauses. Auricular rate 294, ventricular rate with 4 to 1 block 73, with 3 to 1 block 98.

April 17, 1922: The ventricular and pulse-rates both perfectly regular, rate 78. E. C. G. 1671 shows auricular flutter, with a 4 to 1 block. Auricular rate 312 and ventricular rate of 78. It is interesting to note the increase in the auricular rate coincident with digitalization. Patient has no symptoms of heart failure now at rest.

April 25, 1922: Patient's heart and pulse have remained regular until today. This morning it was noticed that they were wholly irregular, with a rate of 78. There was no pulse deficit. E. C. G. 1687 shows that the auricles are now fibrillating. It is also interesting to note how the intraventricular block disappears after the longer pauses.

May 1, 1922: Patient sitting up, feels well. E. C. G. shows auricular fibrillation persisting with well-controlled ventricular rate. Intraventricular block shows in only three complexes.

May 13, 1922: Patient discharged to the cardiac clinic. Ventricles still fibrillating. E. C. G. taken today, 1701, shows that the intraventricular block has entirely disappeared.

Subsequent Course of This Patient.—He was under constant observation until his death, December 5, 1923, one year and seven months after first coming under our observation. During the first year after his discharge from this stay in the hospital he was able most of the time to be up and around,

but unable to work. The last seven months of his life he was confined to a chair or the bed. His auricles fibrillated until death; about three months after this discharge his intraventricular block reappeared and remained until his death.

Discussion of the Case.—We failed to make a diagnosis of auricular flutter on this case until after we had seen the electrocardiogram because of lack of experience and insufficient observations.

He was the proper age for flutter.

He had arteriosclerosis, in which flutter is frequently found.

He readily gave a previous history of previous attacks of palpitation.

The character of the present attack should always make one suspect flutter in a patient at the age of this man.

His ventricular rhythm was regular and the rate one most usually finds in flutter. It was constant.

His pulse was regular except for pulsus alternans, a frequent finding in flutter.

Vagal pressure was not attempted until after the diagnosis was made; it increased the block and was accompanied by a marked slowing of the ventricular rate, which quickly returned to normal when the pressure was relieved.

Flutter waves were not looked for in his jugulars. At that time I did not know that they could be seen.

The case is interesting also because it shows concomitant with digitalization a gradual increase in the auricular rate, until this rate becomes so rapid that the auricle no longer responds as a whole, and fibrillation succeeds flutter.

Case II.—H. N., a driver, aged sixty years, born in U. S. A., admitted to Ward B6 September 8, 1922; been under observation since January, 1922.

Chief Complaints.—Attack of palpitation, dyspnea, and swelling of the feet and substernal distress.

Family History.—No bearing on the case.

Previous History.—Beer and tobacco in moderation all his life. Had scarlet fever as a child; fractured skull twenty-five years ago. Pleurisy fifteen years ago. Venereal denied.

Present Complaint.—For past twenty-five years patient has had sudden attacks of palpitation; during these his heart would beat rapidly for some

minutes and then, as suddenly, the palpitation would stop. These attacks at first gave him no discomfort, nor did they interfere with his work. Twenty-one months before admission (January, 1921) patient's feet became swollen and he became short of breath for the first time. He was put to bed by his physician, who gave him medicine, and in two weeks he was much better. He did not return to work for two months. When he did return to work he was able to keep at his work until nine months ago (January, 1922), when he again developed edema and dyspnea. He went to the Cardiac Clinic at that time, and his occupation was changed to that of a watchman. During the past nine months his attacks of palpitation have become more frequent, and have lasted longer. During the attacks, too, he began to notice a substernal distress and dyspnea, which had not accompanied the attacks previously. Two weeks ago his ankles again became swollen, and last Friday night (September 6, 1922), at the Cardiac Clinic, he was very short of breath, complained of rapid heart-beat, of substernal distress, and of frequent cough. He had a ventricular rate of 158, perfectly regular; he was electrocardiographed and advised to enter the hospital. The electrocardiogram was similar to electrocardiogram 2037 except that the rate was slightly faster, auricular rate 315.6, ventricular rate 157.8. It is not shown because of lack of space. He did not enter the hospital that day, but went home. As he felt no better he applied for admission to the hospital Sunday, September 8, 1922, complaining of palpitation, substernal distress, dyspnea, edema, and cough.

Notes from physical examination by Dr. DeGraff showed: Male, about sixty, with moderate dyspnea and orthopnea; eyes, pupils react to light and accommodation; chest, barrel shaped, signs of congestion at both bases; heart, unable to locate P. M. I. or to define border because of emphysema, sounds fair quality, rhythm regular, rate 156; a blowing systolic murmur is heard at the apex, transmitted into the left axilla; pulse, marked pulsus alternans, frequently every other beat fails to come through, marked sclerosis on radials, brachials, and temporals; abdomen, liver palpable, 10 cm. below ensiform, not tender or pulsating; extremities, moderate edema; retinal examination shows arteriosclerotic fundus. Provisional diagnosis: Arteriosclerotic heart disease, auricular flutter, Class III.

Patient was put on cardiac régime, rest in bed on back-rest, simple diet, and fluids limited to 2000 c.c. for twelve days, during which time he improved considerably, losing 5 pounds in weight, his edema getting less; all of the time he ran a continuously high ventricular rate. During this time the following laboratory examinations were made: Urine: amber, specific gravity 1022, albumin negative, glucose negative, no casts. Blood chemistry: N. P. N. 26.5, creatinin 1.4; red test, 40 per cent. in two hours. Wassermann negative to both antigens.

On September 19, 1922, at 10 A. M., the following note was made: Patient sitting in bed on back-rest, looks comfortable, no cyanosis, no dyspnea, little if any orthopnea, apex not visible or palpable, outlines of heart hard to percuss because of emphysema. First sound of apex heard with maximum intensity in sixth interspace $14\frac{1}{2}$ cm. to left of midline. Rhythm perfectly regular, rate 136. Very faint systolic murmur at apex. A2 > P2, neither second sound is loud. Veins of neck not dilated. Liver not palpable, very

slight edema of legs. On vagal pressure, right or left, patient shows marked slowing of ventricular rate. See electrocardiograms 2037 and 2038.

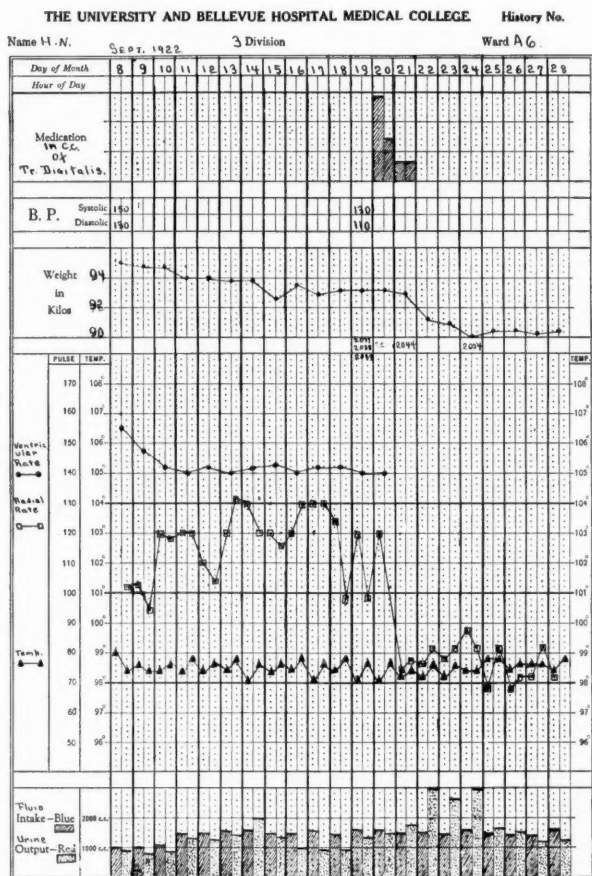
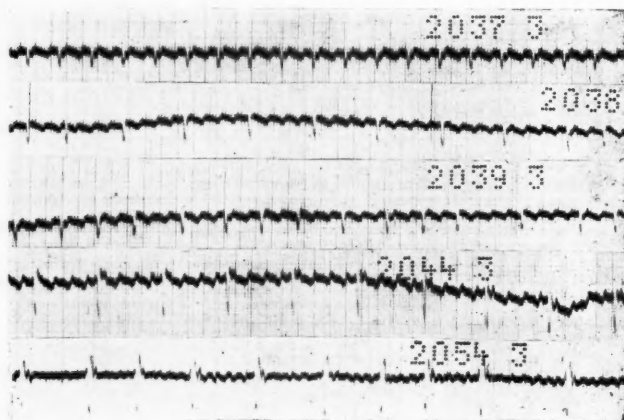


Fig. 89.—This chart shows the persistent ventricular rate as taken by the ward physician, as contrasted with the pulse-rate taken by the ward nurse. It also shows the fall of ventricular rate, decrease in weight, and increase in urinary output following digitalization.

Later in the afternoon the patient was again seen. His ventricle was irregular, rate 110. I thought that he might be fibrillating, but E. C. G. 2039,

taken at this time, showed that his block, which had been 2 to 1 on previous E. C. G., had changed to a varying block. On December 20th the patient was given digitalis as follows: Noon, 14 c.c.; 6 P. M. 7 c.c.; midnight 3 c.c.; December 21, 6 A. M., 3 c.c.

The next morning he was greatly improved; his ventricular and pulse-rate were 70, and perfectly regular. An E. C. G. (2044) taken at that time showed auricular flutter, with 4 to 1 block. Auricular rate 280, ventricular



Figs. 90-92.—Electrocardiograms from Case II (Leads III only shown):

2037, September 19, 1922. Auricular flutter 2 to 1 block. Auricular rate 292, ventricular rate 146. (Similar E. C. G. taken September 6, 1922, auricular rate 315.6, ventricular rate 157.8.)

2038, September 19, 1922. Showing effect of vagal pressure, increasing the a-v. block from 2 to 1 to 4 to 1.

2039, September 19, 1922. Auricular flutter with varying block.

2044, September 21, 1922. Auricular flutter with 4 to 1 block (after digitalization). Auricular rate 290, ventricular rate 72.5.

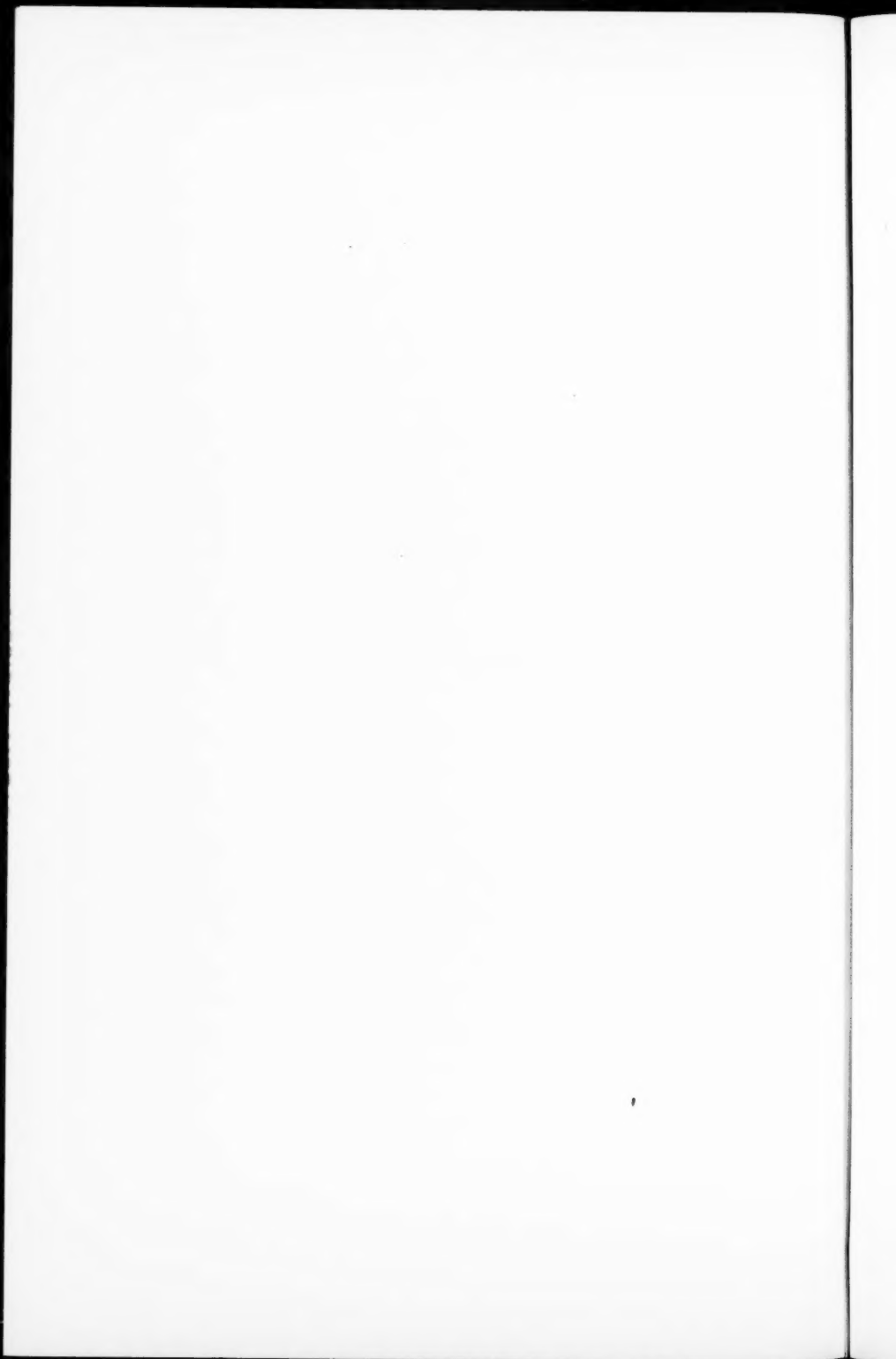
2054, September 24, 1922. Auricular fibrillation. Ventricular rate 72.

rate 70. During the next three days he steadily lost weight. On February 24th his ventricular rhythm became wholly irregular and an E. C. G. (2054) showed him to be fibrillating. The patient was discharged October 1, 1923.

Subsequent Course.—The patient has been under constant observation at the Cardiac Clinic since that date. He is working steadily as a watchman, and has had no further attack of heart failure or of palpitation.

Summary of Case.—Clinical diagnosis of flutter was made on history of attack of palpitation, substernal distress, age of

patient, presence of arteriosclerosis, ventricular rate within flutter limits, persistence of rate whether at rest or at exercise, slowing of ventricular rate by vagal pressure. The irregularity of the ventricular rate on February 18th and 19th might have been thought to have been due to a temporary cessation of the flutter, but the E. C. G. showed that it was due to increased a-v. block. The flutter changed to fibrillation after digitalization, which rhythm has remained to the present time.



CLINIC OF DR. BLAKE F. DONALDSON

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THE TREATMENT OF OBESITY

ACCORDING to Lusk, systems of diet for fat people should be based on the knowledge that a loss of protein is highly undesirable, while a gradual loss of adipose tissue may be a great relief.

The results of treatment in 109 cases of obesity, with a relatively high protein and cellulose, low carbohydrate, and fat diet, will be offered for your consideration.

Of the many problems awaiting solution in the study of obesity, one of the foremost is that of defining normal weight. The life insurance investigators note a difference between average weight and optimum weight. Our figures are based on the average weight charts of the Medico-Actuarial Investigation of 1912. These figures are unsatisfactory in many respects. Many uncomplicated cases of obesity and certain of the frequently associated arterial hypertensive cases fail to reach maximal subjective and objective improvement until reduced below the figures given for their respective ages and heights. I question very much whether it is desirable to steadily gain weight in the next two decades if normal at the age of thirty years. Until something better offers, we have decided for future work to use as a standard the optimum weight table devised very recently by the Statistical Bureau of the Metropolitan Life Insurance Company. This is as follows:

Note that this table is also somewhat unsatisfactory. The figures from 20 to 29, although optimum as to mortality rate, especially from a tuberculosis standpoint, could probably be satisfactorily reduced somewhat. And then, too, no account is taken of the types which Stockard has described in a Harvey

lecture. All ordinary persons fall more or less exactly into two groups, which may be termed the "linear type" and the "lateral type." The linear type is the faster growing, high metabolizing thin but not necessarily tall group, while the lateral type is slower in maturing and is stocky and rounder in form.

**Weights in Pounds Corresponding to 100 Per Cent. Mortality
According to the Medico-Actuarial Table, for Each Inch
of Height.**

HEIGHTS		WEIGHTS ACCORDING TO AGE PERIOD									
Feet	Inches	20-24	25-29	30-34	35-39	40-44	45-49	50-53	54-56	57-59	
5	1	144	137	131	129	128	130	131	130	129	
5	2	149	141	135	134	133	135	135	135	134	
5	3	153	146	141	140	139	141	141	141	140	
5	4	158	151	147	147	146	147	147	147	146	
5	5	163	156	153	153	152	154	154	154	152	
5	6	166	160	159	159	159	160	161	161	161	
5	7	168	164	164	164	165	166	167	168	168	
5	8	170	167	168	169	170	172	173	175	175	
5	9	173	171	171	173	174	176	177	179	180	
5	10	176	175	175	176	177	180	181	183	184	
5	11	*176	*176	*177	*178	179	183	185	187	189	
6	0	*176	*176	*179	*180	181	186	189	190	192	

*At these heights and ages, all weights are over 100% mortality. The weights given are approximately the best weights for each height and age and correspond to a varying mortality ratio up to 110 per cent. of the Medico-Actuarial Table.

Weight, less edema if present, 10 pounds in excess of the average, has been chosen here as evidence of obesity.

Clinic patients with obesity on admission are subjected, after a history is taken and physical examination is made, to

what is known as "obesity routine." They have made an examination of a twenty-four-hour urine, a chemical blood analysis, which includes quantitative hemoglobin estimation, a blood-count, a Wassermann, and a basal metabolism estimation. Until recently we have been attempting to pick out possible potential diabetics in the group by glucose tolerance tests. The lack of uniformity in the results obtained in both normal and obese individuals is discouraging, and the test has been abandoned. Upon completion of the tests the patient is reconsidered as to average intelligence. According a stupid, obstinate patient the medical care necessary to careful loss of weight is a sheer waste of time.

The commonly known dangers of obesity are discussed with the patient, bringing out the increased susceptibility to diabetes, arteriosclerosis, arterial hypertension, cardiorenal disease, and the danger of pneumonia.

An effort is made to dissuade the patient from his own ideas as to the cause of his obesity. He almost always blames heredity for excessive absorption of food from the intestine, or for incomplete combustion afterward. He, if a case of exogenous obesity, is told in simple language that he cannot blame heredity for more than impaired judgment and carelessness as to personal appearance. Also, that there is no evidence of a decreased amount of any internal secretions in his blood. The patient is then given a printed copy of the following régime:

HIGH CELLULOSE AND ANIMAL PROTEIN, LOW CARBOHY-
DRATE, AND FAT DIET

Breakfast:

One orange.

Kellogg's cooked and crumbled bran (1 bowl—4 tablespoons—with milk and either $\frac{1}{2}$ of a dead ripe cut up banana, or $\frac{1}{2}$ of a Shredded Wheat

Biscuit, mixed in with the bran.

Two soft-boiled eggs.

Beverage: Water, or coffee, or tea, or Kaffee Hag, with milk, but no sugar.

Midday and evening meal:

Bouillon, if desired.

Lean meat, chicken, or fish. No thickened gravy or creamed sauce is permitted.

Two vegetables, any kind desired except potatoes. Very little butter should be used in preparing the vegetables. If only one vegetable is available, a double portion should be eaten.

Cheese, if desired.

Raw fruit, or dried fruit, cooked without sugar, or baked apple.

Beverage: Water, or coffee, or tea, or Kaffee Hag, with milk, but no sugar.

Especially avoid:

Bread in any form (this includes toast, brown bread, whole wheat bread, bran muffins, and crackers), butter, sugar, potatoes, olive oil, macaroni, the fat part of meat, candy, any dessert except fruit.

Walk forty blocks (two miles) at a brisk pace, without stopping, in at least forty minutes, and, better, thirty-five, every day.

Certain things are to be noted in explanation of this diet. It has been my experience that the ordinary individual eats much less than commonly accepted standards call for. Particularly is this so of the amount of protein consumed. A 2500 calorie diet is somewhere near the average intake. The proportions in this are about as follows:

90 grams of protein.
100 grams of fat.
300 grams of carbohydrate.

The diet described, when weighed over a considerable period of time by a careful observer, averaged:

60 grams of protein.
30 grams of fat.
125 grams of carbohydrate,
or a total of 1037 calories.

This is well below maintenance requirements. Too far below one would think. Practically, whether because of stolen food, or protection accorded by the relatively high amount of protein, or some unknown factor, the patients do well and avoid a feeling of weakness. Hemoglobin, as a rule, increases. In a few cases we have had to reduce the portions of eggs and meat before a proper rate of loss was maintained. The explanation of this may be that sugar production from meat amounts to 58 per cent. by weight of the meat protein metabolized. This diet has not been used in cases with nitrogen retention in the blood.

Bulk, an important factor, is maintained by giving foods of high cellulose content. The battle, which it most assuredly is, for weight reduction usually comes on the question of bread eating. Any food prepared from flour is forbidden. It seems too concentrated a food for an overweight individual who does not perform a large amount of the muscular work for which carbohydrate furnishes energy. Great difficulty is experienced in getting patients with crippled feet to lose weight. Fast walking, out-of-doors, seems far preferable to setting-up exercises, which will probably be completed in from five to ten minutes. The treatment of exogenous obesity is essentially an ambulatory one if the patient is to retain strength. There is a difference of opinion as to whether any form of special exercise for local deposition of fat is of value. Some good observers, notably Fellows, think that it may be.

Other methods recently advocated for the treatment of obesity have proved successful. Folin and Denis suggest intermittent starvation as a means of reducing weight. The patients are given several fast days, followed by days of fairly liberal diet.

Hawk and Fellows give patients a wide choice of food listed in units of 100 calories. The total amount is kept below 1300 calories per day.

Our results may be summarized as follows:

Eighty-four private patients and 21 clinic patients observed since 1919, who made regular revisits, and who apparently co-operated fairly well in treatment, lost an aggregate of 1339 pounds, or an average of 12.7 pounds per person. The rate of loss averages a little less than 7 pounds a month. Of 4 cases who made revisits, but could not be made to co-operate otherwise, 1 remained stationary and 3 made slight gains.

Endogenous obesity, because of its infrequent occurrence, is a relatively unimportant part of the problem. We have careful basal metabolism work to thank for clearing the air in this respect. In this series we failed to encounter a single case where any proof of thyroxin deficiency existed.

Obesity *per se* does not affect heat production as measured

by the DuBois standards; in 80 per cent. of Boothby's cases of obesity the metabolism was within normal limits, which compares very favorably with the figure of 84 per cent. in apparently normal individuals irrespective of their weight.

Cases with polyglandular insufficiency are usually best treated in the metabolic ward of a hospital. They seldom seem to make marked improvement. Two glands of internal secretion markedly influence the total metabolism. One of these, suprarenal extract, cannot be administered in any way that is of practical value. Thyroid extract, in the dosage of $2\frac{1}{2}$ grains three times a day, is usually absorbed from the intestine in sufficient quantities to increase the basal metabolic rate and to irritate the pace-maker of the heart with resultant increased heart rate. The basal metabolism of proved hypothyroid cases should, if possible, be kept within normal limits by thyroid administration.

The use of thyroid extract in any other than the above mentioned condition cannot be too heartily condemned.

CONTRIBUTION BY DRS. WALTER G. LOUGH AND
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XANTHOMA DIABETICORUM

THAT xanthoma diabeticorum is a rare condition is well established by the fact that an apparently very complete survey of the literature by Major showed a total of 74 cases reported. The series comprised a period from 1848, when the condition was first described by Gull, until 1923. The case for discussion here is not included in Major's series.

Stellwagon describes xanthoma diabeticorum as follows: "A rare eruption observed in diabetic individuals consisting of scattered, sometimes grouped and aggregated, somewhat inflammatory papular or nodular elevations, with usually, in most lesions, the basal portion reddish and the apex of a yellowish or yellowish white, and generally accompanied by slight subjective symptoms of itching and pricking."

The diagnosis of xanthoma diabeticorum must be based on the characteristic skin manifestations, in a diabetic individual with also hypercholesterinemia. Cases of so-called xanthoma diabeticorum without glycosuria are probably not authentic. In addition to the high cholesterol, which is only a part of the total lipoids, the latter are very markedly increased in amounts in xanthoma.

The total lipid content of whole blood, determined as fatty acids, averages in normal individuals about 0.600 per cent., and the cholesterol about 0.14 to 0.17 per cent. With Bloor's method higher figures for cholesterol, about 0.20 to 0.24 per cent., have been obtained, but these are probably too high. The results reported in the table are determined by the method

of Myers and Wardell. Cholesterol is a monatomic, secondary, and unsaturated alcohol, and consequently may form with fatty acids an ester. It occurs in the blood in both a free and a combined state. The free cholesterol is found in the corpuscles principally, and to a less extent in the plasma, but the cholesterol esters are found in the plasma alone. Of the total cholesterol, about one-third is present as esters, and two thirds as free



Fig. 93.

cholesterol. The figures recorded in the table are for the total cholesterol of whole blood.

The total lipoids of the blood include true fats (glycerids of fatty acids), phosphatids, and cholesterol. The total lipoids are determined by the fatty acid content of the blood. The cholesterol content of the blood runs fairly parallel with the total fatty acids in all cases, including severe lipemias. Con-

sequently, cholesterol is usually adopted as the index of the lipid concentration of the blood.

Although within the last few years biologic chemists by their experimental work have greatly extended our knowledge of metabolism in the human body, comparatively little information has been added to our knowledge of fat metabolism. There are many reasons for this; the fats are inert substances



Fig. 94.

and do not readily enter chemical reactions, hence their isolation and identification are difficult procedures. Moreover, the tissues have the ability of storing fat in large quantities, consequently the part they play in the anabolism and catabolism of the body are very obscure. However, these facts have been established. The feeding of fat results in an increase of the blood lipoids, and when large quantities of fat have been taken in the diet,

a lipemia may be observed. This milky appearance of the blood-plasma is due to a suspension of very fine particles possessing brownian movements. The milkiness may persist for from eight to fourteen hours after the fat has been eaten. After an average meal there is no evident lipemia, but the blood lipoids are increased. The lecithin and cholesterol rise along with the true fat, the increase in cholesterol is, however, less rapid.



Fig. 95.

Although there is not sufficient data available at present to justify the statement, there is a definite relation existing among the true fats, lecithin and cholesterol, none the less experiment and observations in pathologic conditions point to such a conclusion, all three classes of blood lipoids are concerned in fat metabolism.

The extent and duration of the increased concentration of

blood lipoids depends upon the amount of fat ingested and upon the level of these substances at the time of feeding. When the blood lipoids are originally high the increase after fat feeding is greater and the decline is more delayed. The mechanism of removal of the fat from the blood is uncertain, but is probably effected through the intermediate stages in which lecithin and cholesterol may take a part. Other foods than fat apparently do not affect the level of the blood lipoids. Fasting may raise or lower the blood lipoids, depending upon the nutritional state of the body. The fat stored in the tissues is derived from two

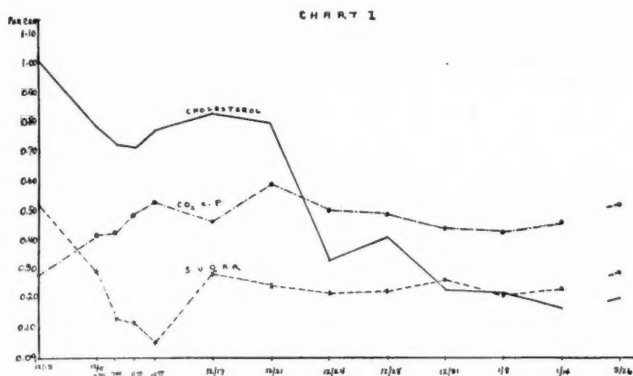


Fig. 96.—Curve showing cholesterol CO_2 and sugar readings after use of iletin and diet.

sources—the fat of the diet and the fat synthesized by the body from other compounds—carbohydrates and probably proteins.

The highest values for the blood lipoids have been found in cases of diabetes. Occasionally the fat content of the blood may be increased to such an extent that a lipemia results. This is not uncommon in untreated cases, and no doubt results from two causes—the fat absorbed from the intestinal tract, and an inhibition of the passage of fat from the blood.

That there is apparently a definite relationship between the hypercholesterolemia and the xanthomatous nodules there seems to be little doubt, but the interpretation of the relationship

will not be attempted except to state that the cholesterol content of the xanthomatous nodule showed 3.48 per cent. by weight, which, in consideration of the fact that cholesterol is very light in weight, seems to be excessive in amount.

The pathologic report of the xanthoma is as follows: "The surface of the skin shows papillæ. It is covered by regular stratified squamous epithelial cells with marked hornification. The epithelial lining is sharply defined from the corium. This layer is densely filled with larger and smaller fat-droplets which show rounded and elongated shape. The droplets mostly are found in the interstitial spaces, occasionally, however, stored in the spindle cells. The fat-droplets take a deep red stain with Sudan III. The deeper layer of the corium is free of fat.

Extensive observations on the chemical blood findings in xanthoma diabeticorum are scarce. Major reports 3 cases, Engman and Weiss reported 1 case, and Nicholson 1 case, all of which showed high cholesterol content in the blood.

The present case is described with the idea in mind to show the effect of iletin on the course of the xanthomata and its relation to the clinical course of diabetes.

The patient, a man twenty years of age, was admitted to the Post-Graduate Hospital the first time in 1922. The complaint at this time was "sugar in urine." There was nothing of importance in the family history.

Past History.—Frequent attacks of tonsillitis.

Habits.—Patient smoked fifteen cigarettes daily; drank 2 cups of coffee.

Gastro-intestinal.—Appetite excessive, always hungry. Constipation marked for several years. No jaundice. No nausea, but eructations of gas.

Cardiorespiratory.—Negative except for slight bronchial cough.

Genito-urinary.—Passes urine every half-hour during the day and about every hour during the night. No hematuria.

Neurologic History.—Entirely negative.

Physical Examination.—Showed nothing remarkable except a very dry skin. Several decayed teeth, large tonsils. Radial and brachial arteries easily palpable.

Laboratory examination showed:

Blood-sugar, on admission, 0.225 mg. per 100 c.c. of blood.

Blood-sugar, on discharge (October 20th), 0.112 mg. per 100 c.c. of blood.

Urine sugar, on admission, 5 per cent., 92.5 gm. in twenty-four-hour specimen.

Urine sugar, on discharge, 0.06 per cent., 1.7 gm. in twenty-four-hour specimen.

General condition of patient on discharge from the hospital satisfactory.

The patient was readmitted in January, 1923 and discharged on February 22, 1923 with blood-sugar 0.123 mg. per 100 c.c. of blood and no sugar in the urine, on dismissal.

Finally, the patient was readmitted for the third time December 15, 1923, with an interval history as follows: After leaving the hospital on the previous occasion the patient broke diet, eating anything he chose. He lost 6 pounds in weight. In September, 1923 the patient noticed an eruption on his skin, appearing first in the lumbar region. The areas would bleed on slight provocation. Subsequently similar elevated areas of a yellowish-brown color varying in size from 3 to 15 milligrams, others up to 20 milligrams, somewhat irregular in shape, sometimes discrete and distinct; then again confluent areas where several smaller ones had coalesced, extending over extensor and flexor surfaces of the arms, the elbows, face, thighs, legs, and a few scattered ones on the abdomen. Photographs will be noted below showing some of the xanthomata. (The chemical and pathologic analyses have been noted above.)

The eruption caused the patient no particular inconvenience except slight itching. It was noticed, however, that healing took place very slowly indeed at the point of removal of the xanthoma nodule.

The general physical examination showed a moderate degree of emaciation. Heart and lungs negative. Blood-pressure low.

The laboratory findings are of unusual interest, particularly as concerns the blood. The blood macroscopically showed the characteristic milky appearance due to the excessive fat, while chemically there was an excessively high blood-sugar and cholesterol and a very low CO_2 combining power. (See Table, page 344.)

Thirty-five units of iletin were administered at 5 p. m. December 15, 1923, with a resultant rapid reduction in blood-sugar, but not a very marked diminution of the cholesterol; in fact, four determinations of cholesterol were made at 3.30, 7, 9, and 10 p. m. the same day, with the fourth cholesterol determination practically the same as the first. It will be noted also (Table 1) that the CO_2 of blood-plasma rose from 28.7 to 49.4, which reduced the incidence of a dangerous acidosis to a minimum.

An acidoses diet consisting of carbohydrate 100 gm., fats 5 gm., and protein 65 gm. was administered with 35 units of iletin in three doses, 15 units at 6 a. m., 10 units at 11 a. m., and 10 units at 6 p. m. After nine days on the above diet and iletin unitage the blood cholesterol had reduced from 0.787 to 0.326 per cent., more than half, while the blood-sugar maintained a fairly high reading, 0.219 mg. per 100 c.c. of blood. The fat was then increased to 25 gm. per day for three days, and then to 50 gm. for one day, after which another cholesterol determination was made, which showed a further reduction to 0.230 mg. per 100 c.c.

Again the fats were increased in the diet to 75 gm. per day, this amount given over a period of about fourteen days, when a cholesterol determination showed a normal percentage, or 0.137 mg. per 100 c.c. of blood, whereas the blood-sugar remained at a high figure, 0.236 mg. per 100 c.c. of blood, but no glycosuria and no acidosis. While the cholesterol returned to normal at a fairly rapid rate the xanthomal nodules disappeared very slowly, and they

TABLE
CHEMICAL CHANGES IN BLOOD AFTER INSULIN AND DIETETIC RESTRICTIONS
Patient A. Y. Age twenty-one. Male. Diagnosis: Diabetes mellitus
with xanthomata diabeticorum.

Date.	Sugar, per cent.	CO ₂ , C. D. per cent.	Choles- terol.	Total fatty acids.	Remarks.
1/10/23	0.302	36.6	0.176	Urea N = 12.5 mg. per 100 c.c.
12/13/23	0.502	28.7	1.072	9.200	
12/15/23					
3.30 P. M.	0.300	41.8	0.787		
					At 5.00 P. M. received 35 units of insulin.
7.00 P. M.	0.134	42.8	0.724		
9.00 P. M.	0.122	49.4	0.720		
10.00 P. M.	0.096	53.2	0.772		
12/17/23	0.296	45.7	0.825		
12/21/23	0.250	58.3	0.792		
12/24/23	0.218	50.5	0.326		Urea N = 10.8 mg. per 100 c.c., chlorids = 0.563 per cent. as NaCl.
12/28/23	0.219	48.5	0.410	
12/31/23	0.262	44.2	0.230		
1/ 8/24	0.206	42.8	0.224		
1/14/24	0.236	46.6	0.137		1.100
3/26/24	0.296	52.2	0.200		

12/31/23: Xanthomatous nodule removed contained 3.48 per cent. cholesterol.

1/3/24: Xanthomatous nodule removed contained 4.33 per cent. cholesterol.

were still present in abundance two weeks after the blood cholesterol became normal

A very remarkable feature was the rapid disappearance of the lipemia, which was very marked at the time the patient was admitted, after feeding fat. This is probably dependent, as was noted above, on the fact that fasting may raise or lower the blood lipoids depending on the state of nutrition, which in this case was very low.

The patient was seen March 26, 1924, when a specimen of blood was obtained which showed a cholesterol of 0.200 mg. per 100 c.c. of blood, and all of the xanthomatous areas had disappeared except one or two small ones on the left elbow.

The treatment of xanthoma diabeticorum is the same as the treatment of diabetes without xanthoma. The skin lesions

disappear as the blood-sugar and cholesterol in the blood return to normal, this more particularly as concerns cholesterol, as the fat metabolism is disturbed more than the carbohydrates, in so far as the xanthomatous areas are concerned. It is difficult to say that iletin has any effect primarily on the reduction of cholesterol. It is more probably the result of the diet and the increased stimulation to fat metabolism brought about secondarily by iletin.

There is no especial need for local treatment, as the skin manifestations are more serious from an objective standpoint, so far as the patient is concerned, than any other way. Furthermore, local treatment would probably be entirely ineffective.

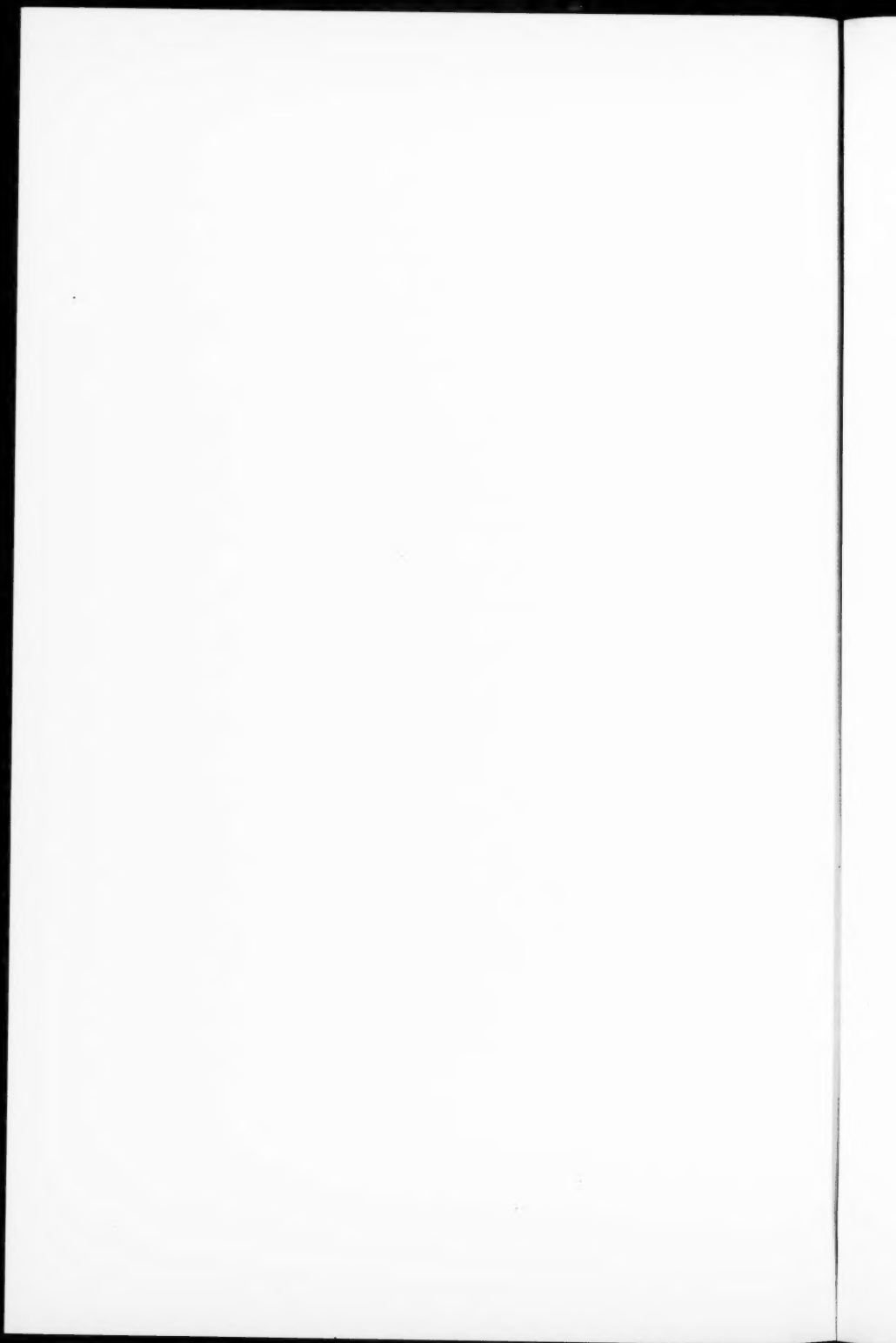
We are indebted to Doctor Klemperer of the Pathologic Laboratory for the report on the xanthoma.

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CLINIC OF DR. MORRIS H. KAHN

BETH ISRAEL HOSPITAL

PULSE DIFFERENCE IN ANEURYSM OF THE ARCH OF THE AORTA¹

THERE are three ways in which aneurysm of the arch of the aorta may interfere with the pulse-wave in an adjacent vessel. An aneurysmal sac interfering between the heart and an artery may (1) act as an elastic reservoir, and, reducing the pulsatile flow, make the expansion and collapse of the artery more gradual; or (2) it may act as an obstruction to the distal artery, its mouth being narrowed by the encroachment of the fibrinous coagulum lining the aneurysmal sac, *i. e.*, thrombosis within the sac; or (3) the outermost coat of the aneurysm may press upon the artery, obstructing its channel and even obliterating it.²

Inequality of the pulses occurred in 13 of 92 history records analyzed by Lamb.³ In a previous analysis of 570 reported cases of aneurysm of the ascending portion of the arch of the aorta, the pulse difference was reported in only 13; in 8 of these the right pulse was the larger; in 4 the left, and in 1 the left pulse was absent in the axillary, brachial, radial, and carotid.⁴

This inequality may consist of simple delay, distinct difference in strength, or complete absence on one side. While this sign appears most common in the radial arteries, it may exist in the brachials or the carotids. Delay is more frequent on the right side, owing to the greater prevalence of aneurysm of the ascending portion of the arch of the aorta.

¹ From the Department of Cardiovascular Diseases, Beth Israel Hospital, New York City.

² Sansum, A. E., *Diseases of the Heart and Aorta*, 1892, p. 134.

³ Lamb, A. R., *Nelson Loose-Leaf Living Medicine*, 1920, iv, 552.

⁴ Hare, H. A., *Amer. Jour. Med. Sci.*, 1899, cxviii, 399.

Associated with this is the difference in blood-pressure on the two sides. Williamson found a difference in the majority of 30 cases, and concluded that a difference of more than 20 mm. suggested aneurysm.¹

From the figures it is evident that pulse difference in aneurysm of the aorta has obtained little observation; graphic records showing this are rarely reported. The pulse difference and the other physical evidence upon which the signs of aneurysm of the arch of the aorta are based is well illustrated by the case here presented:

J. G., a butcher, forty-seven years old, gave a negative family history. His wife and 2 children were well. He had a chancre at the age of twenty-two, but did not remember any other symptoms of syphilis. At the age of thirty-two he had an attack of acute febrile articular rheumatism.

His present illness began six months before he came under my observation, with a dry cough, somewhat "brassy" in character. At the same time he had sticking and aching pain to the right of the manubrium, and also in the right shoulder and scapular region. The pain did not radiate to the left side. Since the onset he had dyspnea on exertion and felt palpitation, not so much in the precordium, as to the right of the sternum.

Physical Examination.—The heart action was regular and of good force. The apex-beat was in the fifth space, two fingers to the left of the nipple line. No murmurs were audible. To the right of the angulus ludovici there was a visible swelling which presented a systolic pulsation. Over this area, 2 inches in diameter, there was dulness to percussion, but no thrill and no murmur. In the neck there were no pulsations and no tracheal tug. The liver and spleen were not enlarged. There were no palpable lymph-nodes and no edema of the feet.

The Wassermann test was + + + +. The urine examination was negative.

Polygraphic tracings taken at the time showed a difference in the radial pulses and in their time relation to the aneurysmal pulsation. This is illustrated in Fig. 97. The radial pulse difference could be felt, the right somewhat delayed. This delay was accentuated when the hands were raised above the head.

Course.—After some months there was increasing cyanosis of the lips and face, with distention of the capillaries on the cheeks. The jugular veins became more prominent. Distended veins appeared across the base of the neck above the sternum. These venous phenomena were more marked on the right side than on the left. The venous distention extended over both arms and shoulders and down to the right half of the abdomen (Fig. 98). The current of blood was definitely in a downward direction in these veins. One branch of the right mammary vein was markedly distended. There were two large veins running vertically over the right pectoral region.

¹ Williamson, quoted by Lamb. loc. cit.



Fig. 97.—Polygraphic tracings showing the time relations between the apex-beat, the aneurysmal pulsation, and the right and left radial pulses. The right radial pulse is smaller than the left and is delayed 0.1 second.

The blood showed a peripheral polycythemia and a hemoglobin reading of 95 per cent.

The dulness in the region of the aneurysm extended from the clavicle down to the third rib. A soft, blowing systolic murmur developed over the heart, heard diffusely, but sharper and higher pitched in the pulmonic area. Later still in the course of the disease there developed a diastolic murmur over the apex and body of the heart and over the pulmonic area. The right border of the heart in the fourth space was 3 fingerbreadths from the median line. The left border in the fifth and sixth spaces was in the anterior axillary

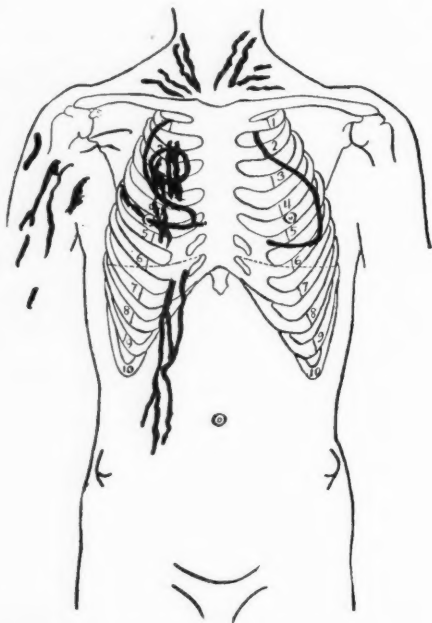


Fig. 98.—Diagram showing the surface outline of the heart and the aneurysm, and the marked distention of the veins of the neck, the superficial abdominal and mammary veins, and those of the right arm.

line. The apex-beat was diffuse in the fifth and sixth spaces. The blood-pressure was 130/90.

Slight puffiness of the eyelids and slight clubbing of the fingers developed, both more marked on the right side. A moderate degree of exophthalmos soon appeared. The pupils, however, were equal and reacted to light and accommodation.

Nine months after the onset of symptoms, and after three months of continued antiluetic treatment, the patient complained of pain which ex.

tended over to the left side of the neck. He walked with a somewhat stooping gait.

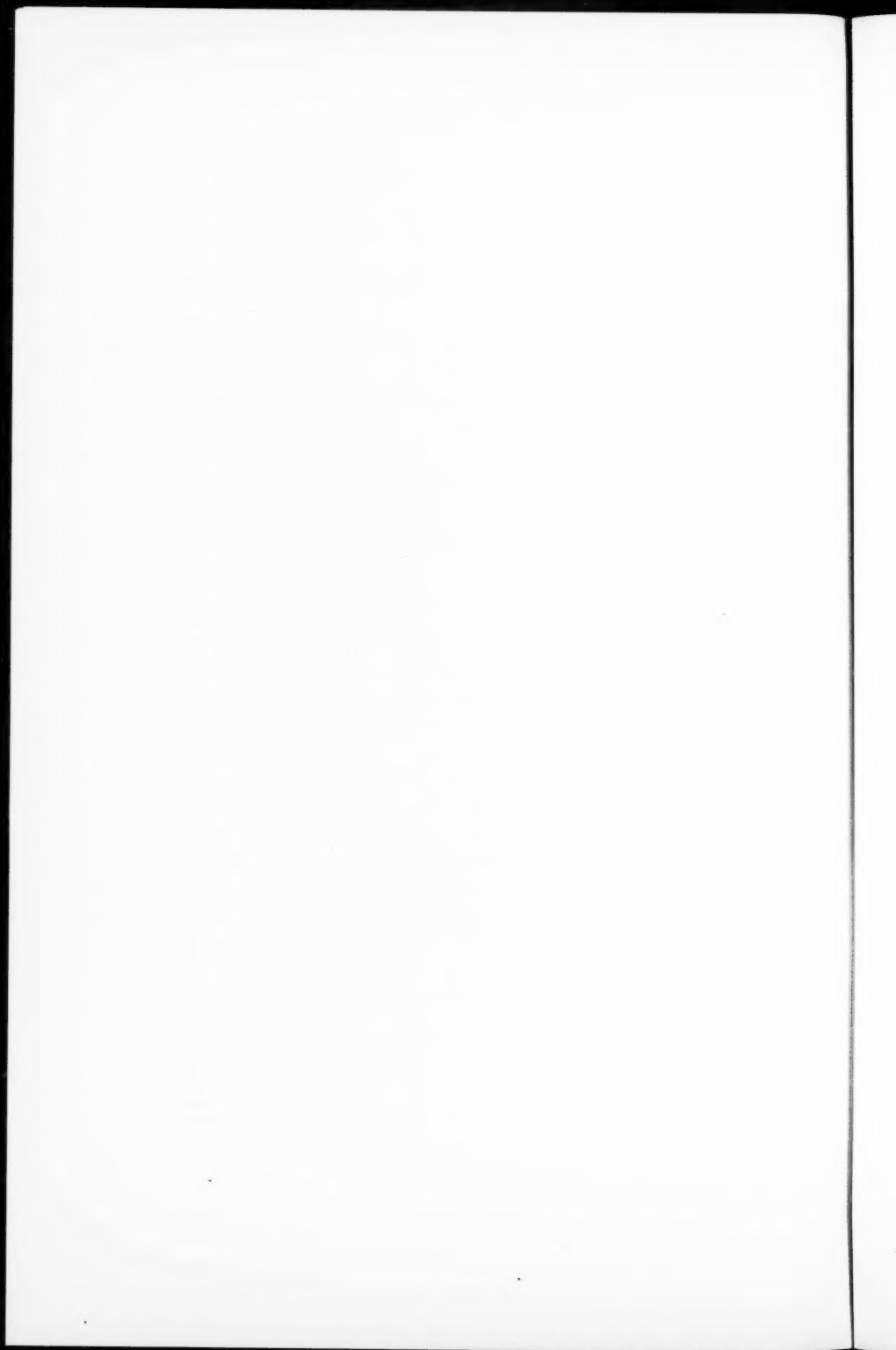
The aortic swelling became larger and its pulsation more distinct. The aortic second sound was markedly accentuated. The supraclavicular regions gave an impression of denseness, but without pitting. The tracheal tug was distinctly felt for the first time. There was no paralysis of the vocal cords.

The lungs showed signs of compression of the right bronchus. Inspiration was sonorous and expiration faint and prolonged over the entire right lung, front and back. Later the right lower lung was atelectatic, while the upper lobe was compressed and showed bronchial breathing. In the left lung breathing was normal. The breathing became grating and audible at some distance. There was almost entire lack of movement of the right chest and compensatory expansion of the left side. On the right side the intercostal spaces were drawn in with each inspiration.

At times the patient had distressing spells of coughing, during which, as he was seated, he became momentarily unconscious, the head sunk forward, the face cyanosed, and the tongue protruded. Except when the patient lay on his right side he was very dyspneic, with "brassy" cough and foul expectoration, and he had a feeling of suffocation, especially in the right upper chest. There was stridulous breathing and profuse sweating of the head and neck.

One week before the patient died the following notes were made: The patient constantly lies on his right side, not otherwise, because of dyspnea and cough. The latter is severe, dry, brassy, and distressing. The patient cannot sleep and can sit up for only a few minutes during the day. He swallows fluids, but does not take solid foods. He complains of pain in the right subcostal region. There is venous distention in the neck and over the abdomen. There is a systolic and a diastolic murmur over the apex and pulmonic area. There is increasing asthenia, gradual asphyxiation by thoracic compression of trachea and bronchi, chiefly the right bronchus.

Death came of progressive cardiac exhaustion.



FROM THE NEUROLOGIC SERVICE
OF BELLEVUE HOSPITAL
NEW YORK CITY

Fits

DR. FOSTER KENNEDY

Multiple Sclerosis

DR. E. D. FRIEDMAN

A Case of Pachymeningitis Spinalis with Thrombotic Softening

DR. JUNIUS W. STEPHENSON

Bilateral Pontine Thrombosis

DR. THOMAS K. DAVIS

Constitutional Inadequacy

DR. GEORGE H. HYSLOP

Spinal Cord Tumor—Three Cases

DR. LEWIS STEVENSON

Multiple Neuritis, with Korsakoff Syndrome, Following Hyperemesis Gravidarum

DR. CHARLES A. CLINE

Some Neurologic Symptoms Caused by Malignant Tumors of the Nasopharynx

DR. L. M. SHAPIRO

CLINIC OF DR. FOSTER KENNEDY

BELLEVUE HOSPITAL

FITS

THE purpose of my discussion today is to say that there is no qualitative difference between one fit and another. There is only a quantitative difference. We are so accustomed to the convulsion associated with uremia—kidney disease— and with the poisonings of an uneasy pregnancy that we have given to these convulsions a special name. We are accustomed, likewise, to the convulsions of childhood, and we think of them in our minds in a special compartment.

It is my belief that all these phenomena properly are epileptic, that epilepsy, as it were, is a spectrum the colors of which merge insensibly the one into the other. At the end of the spectrum we have the major convulsions, with which we are all familiar. Following this we have the convulsions associated with nitrogenous retention in kidney disease; the convulsion associated with disturbed hepatic function in pregnancy. We have the convulsion associated with vasomotor ataxia and with heart-block; we have the convulsions, further along, of the vasovagal attacks, which we should hardly call convulsions, but which are the epileptic states which Gowers called the borderland of epilepsy. We have then the condition of migraine which runs in family stocks, and which often alternates in the same individual with convulsions, and I am not sure but that in the very far, ultra-violet area of the spectrum you will find certain types of hysteric phenomena. This is an iconoclastic statement, I know, because we are accustomed to separate so very closely phenomena which we understand are of the body from phenomena which we think belong to the mind.

Let us have a clear understanding on our part that we are ignorant of the nature of mind. We do not yet know whether mind is a thing in itself, dwelling, as the ministers used to tell us—and some tell us still—in the temple of the body, or whether the mind is a thing of the body, a mere expression of it—a function of the body. If we can clear our own thought that mind is probably a function of the body, we shall see that at least it must operate through an organic mechanism, and that certain hysteric conditions may easily enough be given an organic explanation.

Certain it is that many cases of motor convulsions of a hysteric character have manifestations almost impossible to differentiate from the involuntary movements produced by certain types of midbrain disease. We have all seen certain cases of postencephalitis lethargica in which the incidence of the disease has fallen upon the midbrain, as it usually does—afterward there are rhythmic involuntary, choreiform, athetoid movements of the head. These are not hysteric tics, but are entirely in the nature of release phenomena, that is to say, disordered impulses emanating from the lower motor levels of the basal ganglia, ordinarily controlled by the hegemony of the cortex. When cortical control is interfered with or impaired, there occurs a release of motor impulses from the lower basal ganglia ordinarily subdued by the cortex, and there develop such choreiform, athetoid movements of the head as I have mentioned. These match in an identical degree many hysteric phenomena, and it would seem to me that certain types of hysteric phenomena have a mechanism and produce their quaint appearances by reason of the personality ceasing to operate through the cortex and retreating from a cortical to a lower neuronc level. Many cases of hysteria do operate just in this way, leaving the part of the brain most recently developed and retreating to a part of the brain of greater evolutionary antiquity.

Epilepsy is described by some of the most eminent writers on the subject as an incurable disease, ending in dementia. I believe that, as a profession, we must very strenuously combat

that state of mind. I believe—forgive me for injecting my own ideas so much into this discussion—that epilepsy is a congeries of symptoms, operating no doubt through a common mechanism, probably a disordered, vascular state, a disordered cerebral circulation. The result of this disorder of cerebral circulation is to produce an epileptic fit. That fit comes, as Shakespeare said, in many questionable shapes. It occurs in men for the most part entirely normal, and I very gravely doubt whether 25 per cent. of all individuals do not at some time of their lives have an epileptic seizure of some kind. When I say epileptic fit do not think that I mean a major convulsion, falling down in the street in a tonic state; but I do believe there are not a few of us here today who have had experiences which entirely coincide with Hughlings Jackson's definition of epilepsy. He defined epilepsy, you will remember, as an "occasional, non-volitional, paroxysmal discharge of a nerve center or centers," and I think we must add to this: "accompanied by some alteration in consciousness." I am wording this very carefully you will note. I am not saying "accompanied by some impairment of consciousness."

There are certain states of mental consciousness in which the consciousness does not seem to be impaired, but changed. There is a sense of heightened receptivity rather than lowered receptivity, and one may say this, too, that in the light of the new physics we must not be too sure that our five centers of sense are the only instruments by which we can obtain information, and I would refer you here to a very interesting article by Charles Richet, Professor of Physiology at Paris, which was published in the *Lancet* of September, 1923 under the title of *Extrasensorial Channels of Information*.

I am not trying to be a mystic. I am trying only to tell you that we cannot be too careful in attempting to understand the physiology of our own minds and nervous systems, and that no source of information on their operations is common or unclear.

We have, then, as a definition of epilepsy, "an occasional, violent, non-paroxysmal discharge of a center or centers, ac-

accompanied by some change in consciousness." If you will define epilepsy in these terms you will soon see that it will include a great many convulsive, paroxysmal phenomena—epileptic phenomena undoubtedly—and that they occur in perfectly healthy people as an expression of temporarily altered life processes, and that they do not mean that a person who has had such an explosion is incurable. It does not mean that he will inevitably be liable to recurrent explosions. Neither does it mean that he will be demented in the last instance, and another thing it does not mean is what the psycho-analyst tells us, that such explosions occur only as the expression of a morbid personality.

The psycho-analytic school has flung a very wide net and has brought into that net—or has attempted to bring into it—almost the whole realm of disease; that disease processes are all due to disordered thought processes. Now, it may be quite the other way. It may be that disordered thought processes are due to a disordered physical process. The thought of a man with a full belly is very different from the thought of a man with an empty belly, nor must we be too sure that the tail wags the dog. Certain it is that the claim of the psycho-analytic school that epilepsy is the expression of a morbid, depraved personality, in my opinion, is untrue. We have all known disagreeable and disordered men who have never had a fit, and we have known people with frequent epileptic convulsions of peculiarly sweet and stable personalities. It is a libel on both the well and the ill to say that epilepsy is an expression of morbid, depraved personality.

In this connection I point here to the writings of a very well-known physician of the psycho-analytic school, whose written statements (and this one which I mention here in particular) are exemplars of the things which are being said about epilepsy. It is too long to read in its entirety, but I quote here the original kernel of the idea:

"We are justified in considering the essential nucleus of the epileptic fit an infantile unconscious striving of displeasure-pleasure pursuit ending in the final goal of a return to infancy, attended by a loss of consciousness and a

convulsion; that the convulsion is made up of and flows out of the general striving of the fetal and infantile tissues as expressed through the lower spinal centers in inducing simple and crude combinations of impulsive movements; that a study of the degree of development of unconscious infantile strivings in the emotional instincts, the desire for an infantile state of omniscience (sic) are paralleled by the kind and character of impulsive movements found in this infantile period of neuromuscular development.

"The epileptic reaction, from its mildest to its severest manifestation, is really a protection, for it obliterates reality and reduces the subject to the lowest level of organic response—that of the comatose state. It dispels an intolerable demand, and the epileptic retreats to a state of harmony and peace; gives us a more rational understanding of the nature and mechanism of the disorder itself and renders the plan of handling and treating the essential disorder more understandable and practicable."

This first paragraph, you will see, makes no sense, except that it perhaps indicates the necessity for the unhappy individual to commit occasional psychologic suicide in order to get rid of the horrid awareness of himself which the psychoanalyst says he has. One might say, why should a distraught nocturnal epileptic have to retreat from the realms of unconscious slumber into the realm of epileptic coma in order to obtain psychic tranquillity for a moment or two?

I feel that I ought to state very clearly my feeling on this dragging in of nebulous, so-called "personality states" to explain these phenomena. These phenomena are, as it seems to me, definitely organic, though very difficult to understand. They have a common identity in their manifestations. They are of a protean character, but they can undoubtedly be caused by many forms of irritation producing a vascular ataxia. For example, the cases of Stokes-Adams disease. Lewis showed that a period of asystole of from three to seven seconds' duration was enough to produce impairment of consciousness. That if it were maintained for fifteen seconds a fit occurred: facial twitchings occurred, the corneal reflexes were lost, and a state of tonicidity took place. There is certainly no "personality" defect in this.

What occurs in an epileptic fit? We all know the stages of an epileptic seizure. We see a person—50 per cent. of them—with an aura of some kind, that is to say, a warning that some-

thing is going to happen to him, then, whether he has an aura or not, the fit comes swiftly, instantly, and he falls to the floor unconscious and rigid. His head is thrown back, the arms are thrown out, the toes pointed, the back arched, sometimes, though not always; and a higher state of muscular tonus exists, a rigidity, in which time the individual is cyanosed because of the absence of any breathing movement. Then there occur gradually clonic movements, slowly increasing, then dying away, then recovery. I believe we have all been taught that epilepsy is a disease of the cortex; that these fits occur from cortical irritation, but I would put before you a rather novel idea, that they are due not to a cortical explosion in the first instance, but rather to a sudden removal of all cortical function.

We do not know whether consciousness lives in the cortex or not, but we get a sudden loss of consciousness upon this withdrawal of cortical function, and we find the individual turned into a typical decerebrate specimen. The first stage of the attack is distinguished by a certain tonic rigidity, as though you had drawn a knife through the basal ganglia, allowing to flow from the basal ganglia an unmitigated, ungoverned stream of tonic impulses throwing the individual back into this decerebrate posture. The clonic convulsion I believe has been given vastly more attention than it deserves, as to me it seems to be really a recovery from the fit. It is due to a recovery on the part of the cortex and a resumption by the cortex of the control which it had lost, but not yet volitional. The mechanism that will bring this about must be sought in the circulatory system. I believe that we shall find some day that epilepsy is a disease of circulatory control, and that this, at least, is the common channel by which the fit is produced, and that the reason we have such a spectrum, such a curious number of kinds of attack, is that the cutting off or withdrawal of cortical function is not always complete. It is complete in the *grand mal* attack; it is very incomplete in the *petit mal* attack. All the variations in epilepsy are due, I believe, to the fact that the temporary vascular disorder is complete or incomplete, and if we may see a fragment of a decerebrate rigidity in a partial lesion of the

basal ganglia, so may we also see, in different epileptic phenomena, fragments of the great fit. All these fragments are cutoff pieces from the great jig-saw puzzle which we can understand clearly when we see the whole fit, which, when we see but an isolated part of it, puzzles us, when we do not recognize it for a piece of a great whole with which we are all familiar.

Take, for instance, the case of a friend of mine, a taciturn fellow. He came down one morning—he was always silent at breakfast—looking at me with a curious startled expression. Propping the morning paper against his teapot, he began to try to read. In a moment he changed the position of the paper, turning it upside down, with halting movements, and then, moistening his lips, he began to speak in a very hesitating way. He was aphasic, alexic, and when I came to examine him he was hemianopic. He had numbness in his right hand. This lasted for two hours and was followed by a desperate headache on the left side of the head. The whole attack, headache and local cerebral phenomena, lasted five hours, after which he vomited. During those five hours except for the first half-hour he behaved in a normal way, his aphasia and alexia lasting only during the beginning of the attack. When it was over, however, he had no memory of anything except his entry into the breakfast room, having forgot en all that had happened since. It does not seem very difficult to see the identity of such phenomena with epileptic phenomena.

A young man was admitted to my service at Bellevue Hospital some three or four years ago with the story that every time he heard a sharp sound he fell. I thought him hysteric, and as he walked across the ward I slammed a door. He went down as though he had been struck by a hammer, striking the floor and gashing his chin. He picked himself up at once, wiping the blood from his wound. I had known of his condition for eighteen months previously, but had never seen one of his attacks. When he did this I knew he was not hysteric, and after the occurrence of several major attacks, all produced by sudden sounds, I knew that his case belonged to the epileptic category of acousticomotor type. The first time he had had

an attack was when he was about fifteen. He was a student at school, standing at the blackboard working on a mathematical problem, when the chalk in his hand suddenly broke, making a sharp, cracking sound—such an example for the Freudian of a sly subliminal mitigation of fate—and down he went. Following this whenever he walked along the street (he lived in a village) and heard someone whistle behind him, or heard the sudden, sharp sound of a horse's hoofs near by, he went down. When he came to the hospital we could find no organic signs, nothing abnormal in his reflexes.

We found, however, that he had had a right *caput succedaneum* at birth, and that as a baby he had had infantile convulsions (information we elicited from his mother). It was noted that whenever he fell, or dropped to the ground, his left knee always crumpled under him, giving way before its fellow. I asked Dr. Hartwell to open the right parietal area. There was an old thick, laminated clot over the cortex on that side. It was removed—this remnant of his infantile disorder. Since that time he has been extraordinarily well. You could not find a more perfect example of an apparently functional disturbance, hysterically sounding attack, with a more definite organic cause, nor could you find anyone with a much sweeter personality than this youth.

Before concluding, however, I would like to say a word about one kind of attack with which I came much in contact when working on the symptomatology of temporosphenoidal tumor. Tumors of this area often produce what Hughlings Jackson called the voluminous mental states, a feeling of expanded consciousness, a sense of unreality, a state of consciousness in which the individual knows what is surrounding him, but in which the relationship between himself and his surroundings seems changed; he feels about to know something of the unknowable—as though a veil were going to be torn away. We call these “dreamy mental states.” They occur in many normal people. I suppose there are a good many here today who have had just such things. There are references to them all through English literature. They occur in normal per-

sons, but when a person complains of these states and has an organic cerebral disease, you will almost always find this disease in the temporosphenoidal lobe. This is a minor type of the attack. What might be called a major type is a feeling of dreamy distance, almost indescribable, and then a feeling of inexpressible terror, usually referred to the pit of the stomach, then a hallucination—a ghost, or a phantom, or a specter, known for such by the subject. One of my patients in attacks of this kind always saw an old woman dressed in rags, ringing a bell, and the rags stank. You see when this specter came she experienced a bad smell, a discharge from the uncus, so closely associated with the temporal lobe, and so assigned the odor to the figure. These people, it is interesting to note, always know that the figures they see are not real figures, that they are projections of their own minds, but they are frightened none the less.

Phenomena like this are enormously interesting to observe and to speculate about. I have tried to understand why people with a tumor of the temporosphenoidal lobe had ghostly visitors of this kind, and why tumors in no other part of the brain produced them. One might expect them to have visions of this kind with tumor in the occipital region, the center of vision, but this is not so. Flashing lights may appear from such a lesion, but no complex figures. The function of the temporo-sphenoidal lobe apart from word memory, smell, and taste would seem doubtful—they scarcely exist for esthetic symmetry!

It has come to my mind—and a fantastic notion it is—that as each individual in his development from the ovum to the adult passes through successive stages analogous to those evolutionary stages through which the race has passed, and, as in lower animals, the temporosphenoidal lobes so closely associated with the sense of smell subserve mainly intellectual functions; then a time must exist in the earliest period of each one of us when the temporosphenoidal lobes carry intellectual functions later performed by some other more recently and more highly developed area—perhaps the frontal lobes. The temporal lobes would thus be the repository perhaps of archaic memory

pictures incapable of being ordinarily raised to consciousness, but stimulated to resuscitation by disease. Such disease might thus give rise to that curious phenomenon known to the French as the phenomenon of *dejà vu*—the poignant feeling that one had done already, as though in a previous life, that act before. The patient that put these hare-brained notions in my mind was the wife of a Sussex farmer, who in her attack saw always negroes, despite the fact that she was unconscious of ever having seen a colored person in her life. It developed, however, that she had been born in Jamaica, British West Indies, the daughter of an English sergeant who had returned home with his family when the patient was but a few months old.

This is theory, controversial, and maybe not difficult to controvert, but hypotheses are needed to explain the unknown—provided always that we stand ready to replace our theory with a new and better one, until at last the facts themselves are proved and revealed.

CLINIC OF DR. E. D. FRIEDMAN

BELLEVUE HOSPITAL

MULTIPLE SCLEROSIS

WE shall show you today one or two examples of a nervous disease which is fairly common, namely, multiple sclerosis. We shall present the cases first, reserving the discussion of the disease until later. We might say, by way of parentheses, that this disease was at one time considered rare in America, but more recent statistics have shown that probably next to lues of the central nervous system multiple sclerosis is only second in incidence. In a study which was made by Dr. Bernard Sachs and myself a few years ago, of a series of cases from the neurologic services of Mt. Sinai and Montefiore Hospitals, we discovered that the incidence of multiple sclerosis was more than half that of lues of the central nervous system. Our experiences at Bellevue are very much the same. So we see that this disease is not at all uncommon. In Japan it is said to be practically unknown. It is, however, frequently overlooked.

Case I.—The patient was first admitted to Bellevue Hospital on January 7, 1922. He was then a chauffeur, nineteen years old. Single. Native.

Chief Complaint.—Staggering on walking and weakness of both legs.

Family history negative.

Previous History.—Measles and pertussis. He was always delicate and nervous; never seemed to be able to hold a job for any length of time. For the last two years he has had promiscuous sex relations, but denies infection. There has been no serious illness.

His *present illness* began in July, 1921. While working in a newspaper office he noticed that his right hand became clumsy. He could not write well and could not recognize objects in his pockets. There was a dull pain in the right upper extremity radiating from elbow to finger-tips. His right hand was also weak. These symptoms disappeared gradually, and after one week his hand was nearly normal. About August 1st his left leg became clumsy. He "could not feel the floor with his left foot." There was numbness in this

limb. The right hand had gotten better in the meantime. About Christmas time the right leg became involved. He found he could not walk in the dark. He staggered about. His legs seemed weak. He has recently noticed some loss in sex power. No diplopia. No bladder symptoms.

Neurologic Examination.—Visual acuity was diminished in both eyes. Fundi showed nothing definitely abnormal. Nystagmus to the right and left. Other cranials showed no abnormality except for slight tremor of the tongue. In the motor system he showed weakness of the left hamstring and anterior tibial groups. There was slight irregular tremor of the hands, not typical however. Sensory examination showed impairment of vibratory and of position sense of the toes, especially on the left. There was slight ataxia in both upper extremities, but much more definite in the lower extremities. Vibratory sense was lost in both lower limbs. There was diminution of pain sense along the outer aspect of the left leg. Temperature and tactile sense seemed intact. Biceps jerks were equal and active. Knee-jerks were obtained only with the Jendrassik maneuver. Ankle-jerks were feeble. Questionable pes cavus. Abdominals were obtained with difficulty. Cremasterics were present. Gait was ataxic. The Romberg sign was positive. There was a bilateral Babinski sign. Several days later (January 8th) there was noted slight right facial weakness. Lumbar puncture showed that cerebrospinal fluid was under normal pressure: 1 cell, globulin plus. Fehling's reduced. Colloidal gold curve 0000000000. Wassermann negative in the blood and spinal fluid.

January 20, 1922: Patient walks much more rapidly and steadily.

January 26th: Both lower abdominals absent. Joint mobility sense impaired in the left lower extremity. Vibratory sense lost in both lower extremities. Rest of the status as noted. Temperature was normal. White blood-count, 11,000. Polynuclears 69. Lymphocytes 19. Transitionals 8. Eosinophils 4. Red blood-cells 4,820,000. Hemoglobin 82 per cent. Nurse's notes stated that after two weeks the patient became bright, active, and happy, although his gait was still a bit unsteady.

Discharged February 2, 1922, much improved. The only symptom remaining was numbness in the toes on the left.

He was readmitted July 19, 1922. He was now an elevator operator.

Chief Complaint.—Weakness of right leg for three weeks and difficulty in walking.

Present Illness.—During last three weeks numbness and weakness reappeared in the right lower extremity from knee down. The left leg and hand were also involved. Soon after onset he "lost balance." Reels when he walks.

Physical Examination.—General appearance fair. Head normal. Chest negative. Heart negative. Abdomen negative. Right pupil greater than left. Vision 12/15 O. U. Nystagmus to the right and left. Suspicious temporal pallor of disks. Other cranials negative. Motor: Slight weakness of right arm. Tremor of both arms, more on the left. Loss of cutaneous sensibility over lower limbs. Pain perception delayed. Position sense impaired in toes and fingers. Vibratory sense diminished in legs. Recognition of difference in weights impaired. Little sensory ataxia in upper extremities,

but marked in legs. Ataxic gait. Romberg plus. Reflexes: Triceps diminished on right. Biceps diminished. Knee-jerks obtained only with Jendrassik. Ankle-jerks active. Bilateral ankle-clonus. Abdominals absent. Babinski sign positive on both sides.

9/6/22: Difficulty in emptying bladder. Left arm weak. Right leg weaker than left. Tremor of head. Position sense lost in left upper extremity. Loss of pain and temperature sense over lower legs. Position sense diminished in toes. Vibratory sense lost below D 12. Extreme sensory ataxia in left arm. Cannot discriminate weights with left hand. Romberg plus. Gait ataxic. Tabetic athetosis in left hand. Reflexes as previously noted.

9/19/22: Gait a bit better. Joint mobility sense improved. Vibratory sense still lost to level of ribs. Knee-jerks feeble. Ankle-jerks active with clonus. A diagnosis of tabetic type of multiple sclerosis was made. Vision R. E. 20/40, L. E. 20/70. Fields of vision normal for form, contracted for color. Left eye shows little perception of blue. "Retrobulbar reaction" left pupil (hippus). In October we succeeded in demonstrating central scotoma. This became later twice the diameter of blind spot. Vision 20/100. Retrobulbar reaction was later noticed in both eyes. The rhinologist reported: Atrophic rhinitis. x-Ray examination showed diminished illumination of left maxillary sinus. Discharged 1/15/23 in fair shape.

Readmitted 11/11/23: Chief complaint now was weakness of both ankles, diminished central vision in left eye, difficulty in locomotion, paresthesias in left hand and left ankle.

Physical Examination.—Nystagmus bilateral. Pupils oscillate between contraction and dilatation. Vision O. D. 20/20, O. S. 20/50. Optic atrophy in left eye, now definite. Romberg positive. Weakness of the extensors of left wrist and of both lower extremities. Upper extremities, jerks active and equal. Hypesthesia of left hand. Absent abdominals. Babinski more marked on right and bilateral Rossolimo.¹ Unsteady gait. Slight spasticity of lower extremities. Tremor of tongue and left arm. Diminished vibratory sense, especially over right ankle. The ophthalmologist reported left partial primary optic atrophy. Right, incipient. Vision of left eye 20/100, field contracted for colors.

Fourth admission (January 13, 1924).

Chief Complaint.—Difficulty in judging distance with his eyes, weakness of the lower extremities, loss of position sense in the feet. There was also numbness in the lower extremities, weakness and numbness of the left hand, difficulty in locomotion, and diminished vision in the left eye.

Physical Examination.—Right pupil larger than left, both pupils oscillate midway between contraction and dilatation. This is especially true of the left pupil. Nystagmus, optic atrophy in the left eye, hesitant speech, positive Romberg, weakness of the left hand and lower extremities, tremor of the tongue, absent abdominals, bilateral Babinski, more definite on the right, bilateral Rossolimo. There is a suggestion of intention tremor in the right

¹ The Rossolimo reflex is elicited by tapping the plantar aspect of the little toes. It is considered positive when plantar flexion and fanning of these toes occur. It is an accessory sign of pyramidal tract disease.

upper extremity. There are, in addition, disturbances in posterior column sensation (joint mobility and vibratory sense) in the right hand, with sensory ataxia, astereognosis, and tabetic athetosis. There is hypesthesia in the left upper extremity. Gait was spastic ataxic. Patient seemed amiable, cooperative, rational, intelligent, and alert. The general medical status was negative. Four days after admission the patient became bed-ridden. He had previously been able to stand with support. He got rapidly worse and showed signs of a level lesion, which began at D 12 and slowly ascended to D 8. There was complete paraplegia, sensory loss involving all forms below this level, incontinence of urine, girdle sensation referable to the lower dorsal segments, reflex contractions of the lower limbs in the nature of spinal automatism. Ankle-jerks still continued more active. Knee-jerks were absent, bilateral Rossolimo present, slight tenderness of the lower dorsal spine to percussion.

Today (March 29th) the patient is a chair-ridden invalid. He shows motor paralysis of both lower extremities, without fever and without signs of acute illness. He is intellectually quite alert and answers questions very promptly. He has had no emotional disturbances such as sometimes occur in multiple sclerosis (the so-called emotional instability which manifests itself in uncontrollable laughter). Nor has he shown the child-like attitude toward his illness which occurs so often in patients with this disease. He is well oriented. There is a slight tremor of the head. His sense of smell is normal. The right pupil reacts promptly to light and accommodation. The left pupil responds more sluggishly and there is a tendency toward rapid dilatation (hippus). The pupil seems to oscillate midway between contraction and dilatation. This is sometimes called the retrobulbar reaction because it often accompanies retrobulbar neuritis (Marcus Gunn). There is a distinct nystagmus on looking to the left, less marked on looking to the right, but no ocular palsies. (In October, 1922 the patient suffered from transitory diplopia.)

The visual field on the right is normal. On the left there is a considerable enlargement of the blind spot, with a large central scotoma. The right fundus shows slight pallor of the disk. The left shows more marked pallor. Both corneal reflexes are present.

Sensory and motor fifth showed no abnormalities. Facial innervation is normal on both sides. The tongue is protruded in the median line and is not tremulous. The palate innervation is normal.

The trapezius and sternomastoid, innervated by the eleventh, seem to function well on both sides.

Hearing is normal both for high and low tones.

There is a distinct weakness of both upper extremities, more marked on the left and more so distally.

The biceps, triceps, and wrist-jerks are diminished on the right. There is some atrophy of the muscles in this limb, but no fibrillation. Hypalgesia and thermhypesthesia are present in the right upper extremity. Vibratory and joint mobility sense seem seriously disturbed. Tactile sense is preserved.

There is very definite ataxia in the finger-to-nose test, particularly marked in the right upper extremity, but there are both sensory and cerebellar components, the latter is not ameliorated by visual control.

Astereognosis is present in the right hand. There is pseudo-athetosis¹ in this hand when it is extended and the patient asked to shut his eyes.

The abdominal wall reflexes are absent. The knee-jerks are diminished, more so on the right. The right ankle-jerk is present. The left is absent. There are occasional involuntary flexor contractions of both lower extremities which are an evidence of spinal automatism.

There is a bilateral Babinski sign less marked on the left. There is loss of pain sense from D 6 up to and including the sacral areas. The temperature sense is lost from the same level downward. Tactile, vibratory, and joint mobility sense are also lost below this zone.

The patient exhibits incontinence of urine. He is aware of the desire to pass urine, but is unconscious of its passing. There are disturbances in potency. The passing of stools is similarly involuntary. There is a trophic ulcer over the right buttock.

Summarizing, we may say that we have here a patient who for the last three years has been suffering from a disease of the central nervous system which has been associated with at least four remissions and acute exacerbations. Serologic study during his previous stays in the hospital have proved negative.

His illness began apparently with numbness in the right hand associated with weakness in the right upper extremity. This was followed by difficulty in vision, which cleared up after a few weeks. There then developed increasing weakness and numbness in the lower extremities, with gradual loss of the sense of position of the toes, so that he staggered in walking. When we first saw him his knee-jerks were absent. We thought then that he probably was suffering from what has been called the tabetic type of multiple sclerosis.

Why did we say "multiple sclerosis"? For the reason that here was a young adult without a luetic history and with the following clinical signs: Atrophy of the optic nerves associated with central scotoma on the left, muscular weakness in the right upper and both lower extremities, loss of the deep reflexes at the knee, ankle-clonus and positive Babinski sign, all of which indicate multiplicity of lesion.

¹ Pseudo-athetosis is dependent upon the loss of joint mobility and vibratory sense. The hand then "feels for position in space." This is sometimes called tabetic athetosis because in tabes a similar disturbance occurs due to the loss of posterior column sensation.

The combination of marked diminution of knee-jerks with active ankle-jerks and positive Babinski in itself indicates multiplicity of lesion since one must assume a pathologic process in the pyramidal tract as well as a lesion in the reflex arc of the knee-jerk.

The picture we see today is simply a more advanced stage of the disease. In addition, we have the evidences of a transverse lesion of the spinal cord at the level D 6.

Evidently there is multiplicity of lesion. This constitutes one of the cardinal symptoms of multiple sclerosis. The second is periodicity of the symptoms, and this is also present.

Since the days of Charcot the triad which he described (scanning speech, intention tremor, and nystagmus) was deemed necessary for the diagnosis of multiple sclerosis, but we have arrived at the stage where this complete picture is no longer the prerequisite. We do not await the development of this triad before making our diagnosis. The symptoms which we have seen in this patient, together with one or more of the Charcot triad, are sufficient to suggest a diagnosis of multiple sclerosis.

What are the causes of periodicity in the disease? This is an interesting question. The pathologic process at first is not one involving the axis-cylinder, but rather a lesion of the myelin sheath. If one were asked what is the essential pathology of multiple sclerosis, one could say that it is a disease of the myelin sheath, of the fibers of the pyramidal tracts and the cerebellar pathways. Because the disease, at least in its early stages, is essentially one of the myelin sheath, and not one of the axis-cylinder, recovery of function is possible. This return of function has led many to wrongfully confound multiple sclerosis with hysteria because the symptoms come and go much as they do in functional cases, but a careful neurologic examination in any of these cases will always demonstrate organicity at some time or other in the course of the disease. With the successive exacerbation of the symptoms there comes a time when the axis-cylinder also is involved in the disease process, and when this happens the patient goes into the state of chronic invalidism.

He then becomes a chair-ridden or bed-ridden individual. It takes from five to twenty years for this to ensue,

Why do these patients develop central scotoma and temporal atrophy of the optic disk? Phylogenetically speaking, the temporal half is the most recently acquired part of the optic nerve. Its fibers are, therefore, most sensitive and disease manifests itself first in this part of the optic nerve (Brouwer). Besides, foveal vision is carried by the temporal fibers, hence their greater vulnerability. The pupillary reaction in the left eye of this patient wavers between contraction and dilatation because of this marked atrophy. It is interesting to note absence of early disk findings in spite of visual disturbances.

A level lesion in multiple sclerosis is not a very unusual thing, and in a given case it often is difficult to state with certainty whether you are dealing with a level lesion due to compression of the cord or an episode in the course of multiple sclerosis. If we can demonstrate a focus of disease outside of this level lesion, we may be fairly certain that the case is multiple sclerosis. This level lesion may be due to coalescence of plaques or to a meningitis serosa circumscripta (Horsley, Nonne, Marburg).

This patient gives a history of transitory diplopia. If a patient maintains definitely that he has seen double, and he is a young adult without a history of lues, you may suspect you are dealing with a symptom of multiple sclerosis. It is important to differentiate between the diplopia of lues and that of multiple sclerosis. In multiple sclerosis it is due to a more transient and less complete lesion of the nerve. The microscopic lesion may pick out only a few fibers. Therefore frequently, only a single muscle is involved, while in lues the diplopia is due to a plastic exudate at the base of the brain and the lesion of the nerve is more complete. It involves more muscles and is usually more permanent.

It is only in transverse lesions of the cord that you get the urinary symptoms that this patient shows. Usually there is only difficulty in voiding.

This patient shows ataxia in the right upper extremity which

is made worse by closure of the eyes, but even with the eyes open he demonstrates intention tremor. This is an indication of cerebellar involvement.

QUESTION: What is the prognosis as to life?

ANSWER: The prognosis as to life is usually good. The patients may remain invalids for years. They usually die from some intercurrent infection (bronchopneumonia), ascending infection of the kidney, or progressive bed-sores with resultant sepsis.

Q. What is the treatment?

A. The treatment resolves itself largely into the treatment of symptoms (v. i.).

Q. In this patient the pathology seems to be progressive. When does it stop?

A. It is progressive, yet remitting in its course. I would say that the process ceases when the disease is fully developed. In such cases we have weakness of the lower extremities, cerebellar ataxia, intention tremor, nystagmus, diplopia, temporal pallor of the disks, and mild urinary disturbances. In the well-advanced cases we find the Charcot triad (intention tremor, scanning speech, and nystagmus).

Involvement of the cerebellar system is denoted by nystagmus, head tremor, syllabic speech, intention tremor or motor ataxia, adiadokokinesis, and asynergia in gait and station.

Recently the absence of the abdominal reflex has become extremely significant in the diagnosis of multiple sclerosis. Monrad Krohn, a Scandinavian writer, has postulated that there is a pathway in or near the pyramidal tract which carries the cerebral arc of the abdominal reflex. Grainger Stewart has also predicated such a pathway. Modern observations seem to favor this theory that there is a cerebral arc for the abdominal wall reflex in the frontal lobe. Therefore a lesion or a plaque anywhere along the course of this pathway will abolish the reflex.

Q. Are the vegetative centers affected in multiple sclerosis, such as the respiratory and cardiac centers?

A. Not very often. We have seen only one case presenting

marked evidences of disturbed vegetative function, although we have noted tachycardia in a small proportion of our cases,

Case II.—The last case I presented was one of multiple sclerosis exemplifying the so-called chronic remitting type of the disease, even though it was atypical. I shall now demonstrate a much less common type of multiple sclerosis, the so-called chronic progressive type, without much remission in symptoms:

The patient is a painter, thirty-seven years old, a native of Poland, married; he was admitted to this hospital on February 20, 1924. His chief complaints are weakness and unsteadiness of the lower extremities and a burning sensation in the feet. His family history is negative. He had typhoid and typhus in childhood, apparently uncomplicated. There have been repeated sore throats. He was employed in a restaurant for some time prior to his taking up the occupation of painter. During this time he gained much weight. Eight years ago he began the work of painting and wall papering. He was in contact with lead a good deal and his hands were always covered with paint. He had an attack of lead colic about nine years ago; it was associated with diarrhea. Six years ago he suffered from "acute indigestion." At the age of twenty-two he contracted a gonococcus infection, and at the age of twenty-three a sore on the penis which he "burnt out." Only local treatment was instituted.

Present Illness.—His present illness dates back seven years (two years after taking up the occupation of painting), when he noticed a feeling of fatigue in both feet, worse at night and better in the morning. He was given arch support, and this helped him.

About four years ago he noted a burning sensation in the feet, especially in the toes. This was not relieved by local applications, but helped somewhat by exercise. His gait became difficult. The weakness in the legs was progressive, and for the last two years he has had to use a cane. Lately his gait has become so stiff and unsteady that it is very difficult for him to walk. He has had pain along the outer aspect of the thighs and legs. There has been no remission of symptoms. He has had diplopia at intervals during the past year, especially after attacks of indigestion. Urination was difficult. He has been constipated for the past three years, but this was controlled somewhat by diet.

Physical Examination.—As the patient walks you will notice that his gait is ataxic, he walks on a broad base. The entire body, including the head, trembles. He tends to veer at times to one side and at times to the other. This ataxia, which is quite well marked even when his eyes are open, is of cerebellar origin. It is really an asynergia.

His speech is not typically scanning, but it is deliberate. Enunciation is slow. He is quite alert mentally. He does not exhibit outbursts of laughter, though I believe he smiles readily. He is a man of considerable education;

he has acquired fluent knowledge of the English language. He shows no deterioration. He also has a fair insight into his condition.

The pupils react quite promptly to light; the left pupil is perhaps a little smaller than the right. This anisocoria is not typical of the disease. It may be physiologic. The reaction to accommodation is a bit sluggish. There is a true nystagmus, especially on looking to the left. No ocular palsies. The sensory fifth is normal. The motor fifth functions well. Corneal reflexes present. Facial innervation on the right is somewhat impaired. Hearing is apparently intact. Palate innervation is normal. Tongue is protruded in the median line, slightly tremulous. Sternomastoid and trapezius innervation normal. Visual fields normal. No evidence of central scotoma. Fundi practically normal.

Motor power in the upper extremities is normal. In the lower extremities it is a bit diminished. Abdominal musculature normal. Biceps and triceps jerks active, radial jerks active, no Hoffman sign.¹ Abdominal wall reflexes absent. Cremasterics absent. Knee-jerks very active. The ankle-jerks are active. Bilateral ankle-clonus not exhaustible; bilateral Babinski and Rossolimo present.

Sensation.—Pain and temperature sense grossly normal. Vibratory sense is diminished from the anterior superior spine downward. Joint mobility sense apparently preserved. Touch sense normal except for a mild disturbance particularly marked in the distal parts of the lower extremities. No astereognosis.

His chief difficulty is in maintaining erect posture. There is a very slight intention tremor on the right; more marked on the left. No past-pointing; writing somewhat impaired due to the intention tremor. There is motor ataxia in the lower extremities, perhaps more so on the right. Sometimes this is so marked that it results almost in a dancing spasm. There is no adiadokocinesis.

The patient presents a blank facial expression not at all in keeping with his mental alertness. The facies is not quite like that of encephalitis, but it is still placid.

There is a pseudo-Rombergism, really a cerebellar asynergia.

QUESTION: Can you recognize a spontaneous nystagmus?

ANSWER: Yes. If it is spontaneous it is generally congenital. Most cases of nystagmus of pathologic significance are brought out only by voluntary movement of the eyes to either side or upward.

Blood Wassermann was negative. Urine negative. Temperature normal. No stippling of the red cells. No lead line in the gums. It has been two years since this man has done any painting.

A blood-count gave the following results: Red blood-cells 4,800,000.

¹ The Hoffman reflex is elicited in the relaxed hand by pinching the terminal phalanx of the index- or middle finger. It is considered positive when flexion of the fingers and adduction of the thumb occur. The end-result is really a grasping movement. This sign is sometimes obtained in cases of pyramidal tract disease and has been called Babinski of the upper extremity. The writer, however, has seen it also in basal ganglia syndromes and in neuropathic individuals.

Hemoglobin 70 per cent. Color index 0.74. Differential count: Polynuclears 70 per cent. Large mononuclears 10 per cent. Lymphocytes 20 per cent. Spinal fluid, slightly increased pressure. Cell count normal. Globulin increased. Spinal Wassermann negative. Colloidal gold curve 4443332100. The patient volunteers the statement that the spinal fluid was negative on four previous occasions. Twelve blood Wassermanns were negative. Blood chemistry normal (N. P. N. 40. Uric acid 2.5).

An x-ray examination of the spine revealed no evidence of abnormality of the bodies of the dorsal or lumbar vertebrae.

This patient shows the well-developed picture of multiple sclerosis. This consists of nystagmus, pyramidal tract signs, and cerebellar symptoms. The asynergy, the weakness in the lower extremities, the nystagmus, and the sensory changes indicate multiplicity of lesions. The second criterion requisite for diagnosis, that of periodicity, is absent in this individual. In this patient there probably has been not only a breaking up of the myelin sheath, but the axis-cylinders are also degenerated, therefore conditions necessary for return of function are absent. From the progress of the symptoms in this case the axis-cylinders must have been injured early in the course of the disease. The exaggeration of the deep reflexes, the absence of the abdominal wall reflexes, the bilateral Babinski without evidences of multiple tumors or lues, strongly suggest the diagnosis of multiple sclerosis. On account of the patient's occupation a degenerative lesion due to lead-poisoning must also be considered. However, the absence of peripheral nerve or anterior horn manifestations, the mental alertness, the failure to demonstrate stippling of the reds, the absence of the characteristic lead line in the gums, make it unlikely that we are dealing with such a complication of saturnism.

In the series of cases studied by Dr. Sachs and myself, 30 to 35 per cent exhibited sensory changes, involving joint mobility and vibratory sense more than pain and temperature. The sensory disturbances here are of a similar kind. We have noted this on our service here repeatedly.

The bladder symptoms are usually mild in multiple sclerosis because there is little involvement of the gray matter of the cord. It is only in case of invasion of the gray matter that we

have pronounced bladder symptoms. The significance of diplopia which this patient also complains of was discussed in the earlier section of this clinic.

The etiology of multiple sclerosis has not yet been definitely established. According to Marie, it is an infectious disease allied to encephalomyelitis. Others, like Strumpell and Muller, think, it is degenerative in nature. The fact that it begins early in life would seem to indicate that the nervous system, so to speak, is used up prematurely. Oppenheim thought that it was endogenous and toxic. More recently Kuhn and Steiner, who have done a good deal of experimental work on multiple sclerosis, advanced the theory that a spirochete is the etiologic factor. Other investigators (Marinesco, Siemerling) also claim to have discovered spirochetes in fresh sections. Roth, Freund, and Hornowski have stated, however, that their experiments were uniformly negative. This question is still unsettled.

In multiple sclerosis the spinal fluid sometimes exhibits a paretic colloidal gold curve. This indicates to some observers that there may be kinship between the virus of lues and the etiologic factor in multiple sclerosis. The spinal fluid in multiple sclerosis, as a rule, shows very little abnormality. In the series of cases already spoken of there were only 6 or 7 cases in which we found a slight change in the spinal fluid (increased cell count or globulin). Our Bellevue experience is of a similar nature.

Diagnosis.—One must differentiate multiple sclerosis from a number of other diseases. At times it resembles paresis. The psychotic symptoms, however, are not so profound. The speech is not slurring. There is no peri-oral twitching. The absence of positive serologic findings and of pupillary signs will help to eliminate paresis. Cerebrospinal lues is another condition from which multiple sclerosis must be distinguished. In cerebrospinal lues the pupils are much more seriously altered. The serologic findings will be those of lues (more cells, more globulin, and positive Wassermann). The ocular palsies, too, are much more marked in cerebrospinal lues. Finally, the therapeutic test may help in the differentiation. Luetic cases, as a rule, yield to specific treatment.

The combination of pyramidal tract signs and disturbances of posterior column sensation make it necessary for us to rule out subacute combined sclerosis such as occurs in pernicious anemia, leukemia, and all forms of cachexia. However, in these cases the underlying condition, the characteristic blood-picture, the achylia, and the more advanced age of the patient (fifth to sixth decade), the absence of the characteristic remissions will serve to eliminate this form of spinal cord degeneration. In subacute combined sclerosis also there is very little tendency to cranial nerve involvement; the process seems to end at the cervical cord,

Multiple tumors in the cerebrospinal axis can easily be excluded by the absence of a primary focus, the rapidly progressive course of the disease, and the presence of xanthochromic fluid due to invasion of the meninges.

Multiple sclerosis at times has a tendency to assume a focal character. In such cases you must differentiate it from cerebral or cord tumor. If, however, you can demonstrate one or more foci outside the one producing the focal lesion, you are probably dealing with a case of multiple sclerosis associated with "pseudo-tumor."

Freidreich's ataxia must be considered in differential diagnosis. In this disease, however, there is a distinct familial history, the abdominal reflexes are usually preserved, and there are no fundus changes. The course of the disease, too, shows a steady, downward trend without remissions. We find also other evidences of degeneration, such as scoliosis and deformity of the feet.

Some of the subacute forms of epidemic encephalitis might produce a picture resembling multiple sclerosis, but in the former there is usually less marked invasion of the pyramidal tracts and cerebellar pathways. It is interesting to note here that Marie has spoken of some of these cases as acute multiple sclerosis.

There are some cases of multiple sclerosis with tremor which simulate Parkinson's disease. Some cases, too, appear under the guise of tabes. Our first case began in this way. Spiller

thinks that multiple sclerosis sometimes is due to lues, and Marie has also maintained that all cases of multiple sclerosis in individuals over thirty-five years of age are due to syphilis.

A great many cases of multiple sclerosis are treated as hysteria. It is a great mistake to confound multiple sclerosis with hysteria. This error has often been made. Patients with transitory amaurosis have been designated hysteria. On closer examination one usually finds evidences of organic disease.

Function is not carried on by the myelin sheath, but by the axis-cylinder. For this reason if the axis-cylinder remains unimpaired there need be no permanent loss of function. This may explain the ease with which multiple sclerosis can be confounded with hysteria.

Every relapse that occurs leaves the patient a little more incapacitated than he was before, until ultimately he finds himself in the condition which this patient presents today.

Pregnancy, trauma, and acute infectious disease will often aggravate the clinical picture or bring out symptoms in a case that was latent. We have seen 2 cases in which the symptoms of multiple sclerosis became manifest during pregnancy. We have had occasion to observe the rapid development of clinical signs in an individual who underwent intensive training for the purpose of entering the police force. Stieffler has reported similar observations as a result of intensive training of soldiers in the German Army.

Course.—Multiple sclerosis is usually a chronic disease, with a tendency to progressive deterioration in spite of frequent remission of the symptoms. In the chronic cases the downward trend is steady and progressive. The average duration of the disease is from five to twenty years. The acute onset in some of the cases is often only apparent because the prodromal phenomena are frequently overlooked. The remissions may last months, sometimes years. The prognosis with regard to life is not unfavorable. The disease may last decades. Bramwell reported a case of thirty-three years' duration.

It should be borne in mind that very often a remission, especially in early cases, may simulate a full recovery.

Treatment.—Physical exertion should be avoided. Faradic electricity is also harmful. We have no specific remedies for this disease. According to some observers iodids have proved of value. Marburg and others have recommended colloidal silver preparations either by inunction or by intravenous injection. Intramuscular injections of fibrolysin have also been tried. For the tremor hyoscin in small doses has been of service. The greatest benefit apparently is obtained from arsenic given either by mouth or by hypodermic injection.

The recent work on the spirochetal origin of the disease may in doubtful cases justify the treatment with mercury and salvarsan, both of which have been tried by various observers, with more or less beneficial results. Treatment at the various spas with warm baths, massage, and mild exercise is also useful. In severe cases with spastic contractures section of the posterior root, according to the method of Foerster, has been recommended. Constipation in these cases, due to their sedentary life, is often marked. This should be counteracted by means of enemata or purgatives. For the incontinence of urine tincture of belladonna, in 5- to 10-mm. doses, should be administered two or three times daily.

CLINIC OF DR. JUNIUS W. STEPHENSON

BELLEVUE HOSPITAL

A CASE OF PACHYMENINGITIS SPINALIS WITH THROMBOTIC SOFTENING

THIS man is forty-eight years old, automechanic by trade, married, with two healthy children; nativity United States.

The complaint is inability to use the legs and hold his water.

The history of his present illness is as follows, and you must follow closely the chronologic appearance of symptoms, for upon this depends largely the diagnosis.

The patient was admitted to the hospital February 19, 1924. It was on December 25, 1923 that his first symptom appeared, that is approximately seven weeks ago. This symptom was pain. The pain was of a dull character and described by the patient as "deep in." It was located in the axilla and under the costal margin. Associated with the pain was a sensation of constriction, as if there were something tight around that side of his chest. This pain and the tightness were confined to the left side. These two symptoms persisted constantly for three weeks, then the pain disappeared for a few days, to return at intervals, but with less annoyance, finally disappearing entirely, but leaving him with the tight sensation which is present today. His second symptom did not appear until one month after the onset of the pain. That symptom had to do with his left leg, it began to get weak, not suddenly but gradually, and it must be noted that as the pain became less his leg symptom became a source of anxiety. The leg grew progressively worse, but all the while he was at work. Four days ago, however, he awoke from a perfectly normal night's sleep and discovered he had no use of either of the lower extremities and could not "hold his water." It is this condition in which we find the patient today.

His previous history is negative in regard to any previous serious illness, but excessive use of alcohol is admitted, and also a chancre twelve years ago, for which he received a limited amount of treatment. There is no hereditary history.

On examination we find a man with somewhat anxious expression who cannot use his legs and there is the odor of urine. There is no abnormality of the cranial nerves with the exception of the pupils. They are irregular in outline, the left is a trifle larger than the right, there is a slight dead-like haze, but both respond quite promptly to light and accommodation. The upper extremities show no abnormality; the lower are motionless. The

abdominal and epigastric reflexes cannot be elicited. The left knee-jerk is present, the right not elicited. The left ankle-jerk is fairly active, the right not elicited. The left plantar stimulation shows a suspicious extensor response, whereas there is no response on stimulation of the right plantar surface. In testing for sensory disturbance we find on the right side there is a complete loss for all sensations up to the level of the eighth dorsal vertebra. On the left side, while there is a distinct diminution to pain and temperature stimulation, it is not a complete loss. However, on this side his sense of position, that is, his ability to know the position of his toes, is gone. No spinal tenderness can be elicited and there is quite free mobility. No deformity is seen. x-Ray of the spine is negative. Lumbar puncture disclosed fluid under slightly increased pressure, and the analysis showed 100 cells per cubic centimeter. Globulin 2 plus, colloidal gold negative, Wassermann anticomplimentary. Wassermann of blood one plus. No tubercle bacilli were demonstrable in the spinal fluid, and the routine examination of blood and urine was negative. His chest and abdomen have been thoroughly examined and pronounced negative.

Having all these facts, we will now attempt to locate the lesion, after which we shall try to determine its pathology. In locating the lesion several factors will aid us: first, his own description of the pain, it was always in the same place, with the same "tightness," and if you note carefully it corresponds quite accurately with the sixth dorsal posterior root distribution. The description is that of a posterior root irritation or compression, and therefore we feel pretty confident the lesion is in this neighborhood. Second, we cannot elicit the abdominal reflexes, that is, on gently stroking the abdomen we do not get a flicker of the abdominal muscles. Now we know this reflex is controlled by the eighth or ninth dorsal segment, and, therefore, on account of being unable to get these reflexes, the lesion must be at or above the segment controlling these reflexes. We know the upper extremities are normal, and inasmuch as the first dorsal segment has to do with the function of some of the small muscles of the hand, which are shown to be normal, therefore the lesion must be between the first dorsal and the eighth or ninth dorsal vertebrae. Third, in testing for sensation, that is, his ability to feel pin prick and hot and cold tubes, we find on the right side he feels nothing below the level of the eighth dorsal vertebra, and what he feels on the left side is very much diminished. Now we know that the roots extend down-

ward within the spinal canal before they emerge, and usually emerge about two vertebræ below their real location in the spinal cord itself, so you can readily see that inasmuch as we find a sensory level corresponding to the eighth dorsal vertebra, the lesion will be under the sixth dorsal vertebra. So much for the location of the lesion. What is its pathology? There are three possibilities, viz.: Pott's disease, or tuberculosis of the spine, spinal cord tumor, and an inflammatory condition, viz., pachymeningitis. Although Pott's disease must be considered, it is extremely rare for such a pronounced involvement of the spinal cord to make its appearance so rapidly unless there has been a rapid destruction of the vertebra, with a consequent crushing in or luxations of various degrees, all of which are eliminated by the x-ray examination. Of course, were these findings present, we would of necessity find deformity, rigidity of spine, etc., all of which are conspicuously absent. Therefore we feel that Pott's disease is not a factor here. Regarding spinal cord tumor, a tumor on the left side of the cord situated extradurally could account for the symptoms up to the sudden development of his paraplegia. An extradural tumor could give the trouble he had with the left leg and the difference in the sensory findings by pressing directly on the left side of the spinal cord, because we know in the spine the pyramidal fibers do not cross, and therefore what trouble he would have would be on the side the tumor pressed upon. At the same time he would have more pronounced change in his pain and temperature sensations on the opposite side because these fibers (and by the way, they are afferent fibers) cross almost immediately after they enter the cord. Now the fibers controlling the position of the toes do not cross, so that is why, if this is a tumor, that he makes most of his mistakes in the left foot. This phenomenon is what is known as the Brown-Séquard syndrome, and means a half-lesion of the spinal cord. We believe this is what this man had up to the onset of his paraplegia, and, as stated before, could be accounted for by a new growth, but we feel the suddenness of the paraplegia and the marked pleocytosis—100 cells per cubic millimeter, the increase in globulin, the one plus Wassermann,

the history of syphilis, the inequality and irregularity and dead haze of pupils—speaks against a cord tumor and for an inflammatory condition, viz., pachymenigitis hypertrophica. This is a condition usually seen in adults, the causative factors being syphilis, alcohol, trauma, and exposure. It is characterized by fibrinous exudations which become more or less laminated, sometimes forming a complete ring around the cord, at another time forming lineal streaks. As the condition develops they become thicker and thicker, exerting pressure on the roots of the cord, giving rise to pain and motor phenomena, and finally on the cord itself. In the case of the ring formation there is gradual squeezing of the cord, giving rise to a spastic paralysis. In the case of the lineal formation the pressure is exerted on the side of the cord. In this patient we believe the formation to be lineal, and on the left side giving rise first to compression of the sixth dorsal root, and as the exudate became thicker and thicker giving rise to pressure on the left side of the spinal cord, and that during the relaxation of sleep little particles of exudate got into the blood-vessels and produced a thrombotic softening of the cord at the level of the sixth dorsal vertebra. You must recall that what happens in hypertrophic pachymeningitis is that the inflammation attacks the inner surface of the dura mater and that the fibrinous exudations take place between the dura mater and the spinal cord itself, and when you remember what a tiny little space this is you can readily see that it takes only a small amount of exudate to give signs of pressure on the neighboring structures. At times these exudates become so fibrosed as to have the consistence of osseous tissue. We feel that the history of a chancre and the present serology leave no doubt of the syphilitic cause of this man's illness. Active antiluetic therapy will be instituted, but realizing that the quite probable exudate is causing mechanical pressure, we shall also advise that the spinal canal be opened and freed of any exudate, because by this time the exudate is too well formed to be relieved by internal medication.

Now, gentlemen, from a clinical standpoint there are a few minor matters to which we should like to call your attention.

This man admits a chancre twelve years ago. His pupils are not fixed, but they are irregular in outline and of unequal size. They respond quite well to both light and accommodation. The point is, that fixed pupils in syphilis of the nervous system do not develop overnight, but slowly, and an irregularity in outline of the pupil, particularly if associated with an inequality of the two pupils, must of necessity be looked upon as syphilitic until proved otherwise. Now about the "dead-like haze." This is what we call the "dead man's pupil." We call it that because when fully developed it looks like the pupil of a dead man. It is a peculiar haze which at first might suggest an opacity of the cornea or even a cataract or some disturbance of the vitreous, but, unlike these, it is no barrier to an ophthalmoscopic examination, one being able to see distinctly through this peculiar haze. It is present early and is always of very suspicious import. As yet we have no explanation for it, but as a clinical entity we feel it has its place in diagnostic fields. Another clinical fact to which we would call your attention is that syphilis in attacking the nervous system rarely does so *en masse*, but produces symptoms referable to a patch of meningitis here or there, as in this case. In other cases it may be referable to an area in the brain supplied by a small blood-vessel. For example, several years ago there was sent to us a man because he had a four plus Wassermann in the blood. Clinically he was supposed to have been all right, but in taking his history it was learned that three months previous he had suddenly lost the use of his right arm. His serology proved positive in blood and spinal fluid, and before therapy was instituted he suffered a typical apoplectic stroke involving the right side of the body with a motor and sensory aphasia.

Now what happened to this man when he "lost his right arm" was that he had a thrombosis of the artery which supplies the postcentral area of the brain, this being the higher center for the recognition of pain and temperature sensations. It was looked upon as a case of indigestion. It is good policy to look upon all pains with tight sensation and local loss of power as indicative of the fact that there is something radically and organically

wrong with the nervous system, and always bear in mind syphilis, for if these cases are recognized in their very incipency much unhappiness and many tragedies can be avoided. We do not know what we can do for this unfortunate patient, but we firmly believe had his condition been recognized with the onset of his pain he would not be in his present plight. In justification for this optimism we will briefly cite a case seen several years ago. Briefly, he was sent to us as a case of sciatica of seven weeks' duration. He had had pain beginning in the back, later extending down the back of the leg, stabbing, shooting in character, finally requiring morphin for relief. The man was bedridden. He was a man twenty-six years of age, who denied lues or any history of significance. Except for irregular and slightly sluggish pupils he showed no abnormality of the nervous system except that in his left lower extremity. Here it was observed that the muscles of the calf and peroneal group were distinctly flabby (evidence of beginning atrophy); there were also fibrillations, which are fine more or less rhythmic tremors of individual muscle-fibers. The knee-jerk was normal, but the ankle-jerk was very sluggish. Stimulation with pin prick revealed a marked diminution over the outer aspect of the leg area supplied by the second and third sacral roots. The x-rays of the lower spine, hip, and sacro-iliac joint were negative. The spinal fluid showed a four plus Wassermann, 208 cells per cubic millimeter, and a four plus globulin. The blood Wassermann was also four plus. Now when you recall the formation of the great sciatic nerve, namely, by a fusion of the lumbar sacral cord and the upper three sacral nerves, you can readily picture just where the trouble was. The man was showing compression of his posterior roots manifested by the pains and sensory changes and of the anterior or motor roots manifested by the flabbiness, fibrillations, and altered ankle-jerk. Suffice it to say within a month's time of active antiluetic treatment he was free of all pain, his leg showed a distinct rounding out, and his ankle-jerk was nearly as active as the good one. He went back to work, and so far as we know has continued to do well under a continuance of therapy at home.

CLINIC OF DR. THOMAS K. DAVIS

BELLEVUE HOSPITAL

BILATERAL PONTINE THROMBOSIS

AMONG 72 cases of brain softening on a vascular basis, concerning which Dana gives statistics, only 1 case had a pontine localization. This shows the comparative infrequency of vascular lesions in the pons, and Dana further points out that such lesions of the pons alone are rarer than those involving also the medulla, especially the upper part of the latter. This is because the basilar artery is not plugged as often as the vertebrals and their branches. Isolated lesions of the pons vary in location and size, give rise to a complicated array of clinical pictures, and can be worked out in each instance only by painstaking studies of the motor nuclei in the brain stem and of the motor and sensory tracts traversing it. The time now at our disposal will be taken with the examination of one patient, for in this way a start can be made on the subject of pontine localizations.

Case M. D. is a barge captain of Russian nationality. For two years he has suffered from dull frontal headaches, which he has attributed to a concussion in a fall. Nine months ago, while seated at a table in his cabin, he noticed a sensation as if for a moment a veil of darkness was before his eyes. He did not lose consciousness. He then noticed a numb feeling in the tip of his right third finger, and hurriedly procured a liniment and sought to relieve the strange sensation by rubbing his hand vigorously. As he did so he felt the sensation of numbness extend in all the fingers of his hand, and gradually into the arm and the whole right side of the body. With this the upper and lower extremities on that side became weak and paralyzed so that he could not use them, and at the same moment he began to see double. He examined himself in a mirror and found that his left eye did not turn properly. The paralysis had not changed the movement of the right side of the face. He had not lost consciousness. He was taken to his home in an ambulance and remained four weeks in bed. Then strength had considerably returned in the leg and he was able to walk. His double vision improved greatly two or three days after its onset, though the eye remained very mark-

edly strabismic, and he had diplopia when attempting to turn his eyes to the left. Though his arm regained some power, particularly in the distal portions, his ability to use this extremity remained poor. The above episode marks the development of one syndrome, the signs of which we will consider below.

Two weeks ago he was awakened at night with a more than usually intense headache, so that his head felt swollen out like a balloon. After bearing with this pain for a few minutes he attempted to get out of his bed, and discovered that there was a weakness of the left arm and left leg and that the right side of his face was paralyzed. His speech had become somewhat changed and he felt that he could not enunciate clearly. After only a day or two the speech became normal and the power in the left extremities returned to almost normal, but the facial weakness on the opposite side continued very marked. Because of this and a lively apprehension regarding the situation which in less than a year had brought such devastating symptoms he presented himself to the clinic.

This man is only thirty-six years old, though he looks somewhat older. He is a thick-necked man, with a stocky build and wide costal angle. He is big framed and very muscular and has a rather well-marked hypertrichosis over his whole body. His present weight is 185 pounds, and up until two years ago he weighed 212 pounds.

He went to sea when only fifteen and became accustomed to hard work, though five years ago, because of acquiring a wife, he shifted to a less roving life and became a barge captain. His history is negative for any venereal infection and subsequent serology confirms this point. He has taken food in excessive amounts. He has always eaten two restaurant meals (in succession) instead of one, and had the habit for several years of eating at least a pound of meat, often raw, three or four times a day. Not so much this high protein intake itself as the gluttony has been a likely factor in the development of the nephritic condition which he now shows. In contrast to his gluttony he has never used alcohol to any extent and also has been very moderate with tobacco. He has always been free from constipation.

Physical Signs.—The patient walks with a so-called hemiplegic gait. This is because his right leg is poorly managed, and in order to have it clear the floor he imparts to it a lateral swing from the hip as he advances it forward. He does not drag it after him as would a man with a hysteric leg paralysis.

Taking up in sequence the cranial nerves, we find that the first nerve functions properly, also the second. There is good vision, normal fields, and normal appearance of the fundi. Both pupils are properly reactive to light and on accommodation and are equal and regular in outline. There is a paralysis of the left external rectus (Fig. 99). Except for this the ocular movements are properly carried out. We find no changes, either motor or sensory, in the distribution of the fifth nerve. The entire right

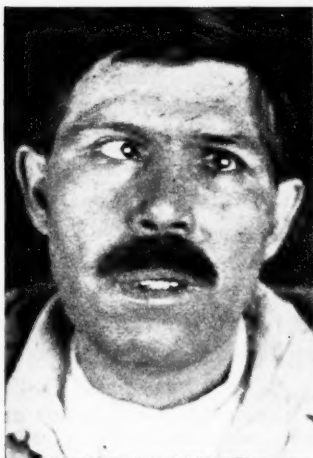


Fig. 99.—Showing paralysis of the left external rectus muscle.

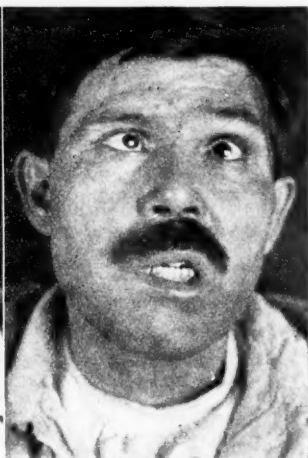


Fig. 100.—Showing the right-sided facial paralysis which includes the forehead.

side of the face is paretic. You note that the upper portion of the face is involved (Fig. 100). The inclusion of the forehead shows us that the injury to the facial nerve on that side has been either in the nuclear or infranuclear (peripheral) portion of the nerve. Later points in the examination will make clear that it is nuclear. If, in contrast, the forehead on that side was not involved in the weakness we would know that the lesion was supranuclear (cortical or subcortical). The patient has no impairment of hearing. There is slight weakness of the

right side of the palate with the palate pulled somewhat to the left. There is debatable weakness of the right side of the tongue. Both of these findings are caused by injury to some of the pyramidal tract fibers traveling to the nuclei concerned, namely, the ninth (the tenth also?) and the twelfth.

Proceeding to the remainder of the body, we find that there is very considerable motor weakness of all his extremities. This is of greatest severity in the right arm, which is rigidly held at the right side and functions almost none at all. The left extremities, relatively slightly concerned, show nevertheless

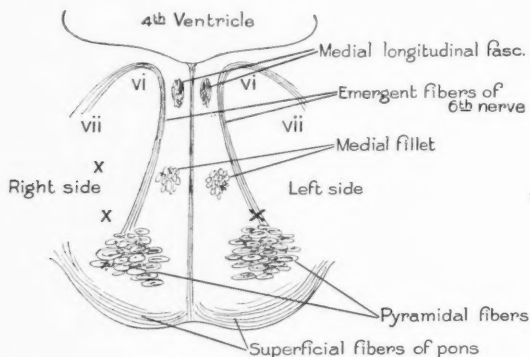


Fig. 101.—Schematic drawing of cross-section through caudal portion of pons. X marks site of lesion inducing right hemiplegia and left external rectus paralysis; XX marks site of lesion giving right facial paralysis and partial left hemiplegia.

very definite reduction in motor strength. In reality, this man shows residuals of a diplegia inasmuch as hemiplegic signs are present bilaterally. In addition, neither has hemiplegia ever been complete, for on each side the paralysis occasioned by pyramidal tract injury left the face, on that basis, untouched. When we speak of this patient's hemiplegia (the right-sided one is now conspicuous) we have in mind the fact that there is an upper motor neuron type of weakness present in the extremities, and to a small extent in the tongue and in some of the muscles of deglutition.

There is general overactivity of all the deep reflexes, combined with a dorsal flexion of each great toe when the corresponding sole of the foot is stroked. This last finding indicates a lesion of the pyramidal tract of each side, as does the fact that the epigastric and upper and lower abdominal reflex is absent on each side. There is also on each side a strongly positive Hoffman sign, which consists of a reflex flexion of the terminal phalanx of the thumb when the nail of the third finger is flicked.

Sensation in all its forms—tactile, thermal, pain, postural, vibratory—is unaltered.

Localization of Each Lesion.—The history shows that with the onset of the right-sided hemiplegia there was a simultaneous involvement of the left external rectus muscle. In other words, there was coincidental injury of pyramidal fibers and a sixth nerve. A single focus for the induction of these changes exists in the caudal portion of the pons in the level at which the sixth nucleus is about to leave the brain stem. We are able, therefore, to localize the lesion which has caused the severer and more long-standing hemiplegia (right) to the caudal portion of the left side of the pons. This lesion reaches the pyramidal fibers enervating the right side of the body and the fibers of the abducens nerve of the left side. Evidence of the circumspection of the lesion lay in the absence of all other motor and sensory symptoms. There is no sensory loss because the lemniscus (the medial fillet) has been spared in the lesion. The vascular supply of this part of the pons lies in pontine branches of the basilar artery.

A more recent lesion caused simultaneously a partial weakness of the left arm and leg and a paralysis of the right side of the face. Here again a single focus exists to cause these simultaneous changes. It also is pontine, but obviously is on the other side of the pons from that of the earlier damage. In this second instance the lesion has seriously injured the right facial nucleus and to a considerably lesser degree the pyramidal tract going to the left side. It is clear that the facial nerve injury was inside the brain stem and was not peripheral, or there would not have been coincident insult to the pyramidal

fibers. These pyramidal fibers descend to the lower portion of the medulla and then decussate. This fact accounts for a brain-stem nuclear lesion, here the damage in the facial nucleus being associated with a weakness of the extremities of the crossed or opposite side. It is an example of a crossed syndrome. All crossed syndromes are due to brain-stem lesions, and in view of the number of brain-stem nuclei, which there are in rather close association with descending pyramidal fibers, the number of possible crossed syndromes is not small. The most classical of these syndromes are those of Millard-Gubler, of Weber, of Foville, and of Jackson.

We have in this patient two examples of the so-called crossed syndromes each arising as a separate clinical event.

The crossed syndrome, which consists of a homolateral facial nuclear paralysis and a contralateral paralysis or weakness of the extremities, is called the Millard-Gubler syndrome. It makes for a little confusion to admit that quite the same name is put down in some text-books for the crossed syndrome which involves a homolateral sixth nerve and pyramidal fibers supplying the contralateral extremities. This apparent confusion is lessened when we remember that each type of Millard-Gubler syndrome depends on a lesion in an almost identical part of the pons, and the differences rest on the relative degrees of injury to two close-lying nuclei, namely, the sixth and the seventh and their emergent fibers.

This particular case is, therefore, found to display two Millard-Gubler syndromes, exemplifying the two types of that syndrome.

Having localized each lesion in the case, it is in order to discuss their nature.

First, because of the abruptness of the onset, the discreteness, the signs induced in each instance, and the early institution of progressive improvement it is fairly certain that the injury in each instance has been vascular in nature. We conclude that neither vascular accident was hemorrhage, for both occurred while the patient was at rest—the second, indeed, while the patient was asleep. This strongly indicates a thrombosis. The

first event had especially clear characters to indicate thrombosis, for during a period of many minutes there was a gradual spread of signs which the patient was able to observe carefully. We do not consider embolism in the absence of any source for this. The cardiac examination is negative, including electrocardiographic record. Our first suspicion in encountering thrombotic disease in a man of our patient's age is syphilis. But the negative blood Wassermann and normal spinal fluid makes us exclude that possibility.

Instead, back of the development of thrombi in this man, is nephritis, hypertension, and arterial disease. The first is shown by the condition of the urine with a cloudy albuminous precipitate and hyaline and granular casts. There is no glycosuria. The specific gravity is 1021. Poor kidney function is further shown by the phenolphthalein test, for there was 25 per cent. excretion in the first hour, 7 per cent. in the second hour, and a total in the two hours of only 32 per cent. The hypertension is considerable. On admission to the hospital the systolic pressure was 215, with a diastolic pressure of 140. After a period of hospital rest both were reduced, the systolic to an average level of 180 and the diastolic to 125. The arterial changes, while no doubt present, are relatively inconspicuous as yet. The peripheral arteries which can be palpated show a moderate degree of thickening of their walls. It is possibly one of those cases in which for a time cerebral vascular sclerosis precedes a generalized arteriosclerosis.

There is good likelihood that the several disabilities now present in this man will show considerable betterment. Even the right (incomplete) hemiplegia, though it is severe and has been present for almost a year, is still improving, and under regular massage and passive movement of the joints more improvement can be procured. The paresis of the external rectus muscles, on the other hand, is total, and in view of its unchanging character for so many months is, we believe, dependent on a complete interruption of sixth nerve-fibers. There is small chance that it will improve.

The comparatively recent facial paralysis is not complete, for

the orbicularis can be partially contracted. It has shown slow improvement and further recovery can be confidently expected. A testing of the electric reactions of the affected muscles shows that they react to both faradism and galvanism, though with each larger currents are required than on the healthy side. The presence of electric responses, even though reduced, further confirms the opinion that recovery of the facial paralysis, possibly almost complete, can be reached. Thus for the immediate future there are prospects of amelioration of the present disabilities. On the other hand, the larger prognosis is very poor. Already in the course of one year two serious vascular accidents have occurred due to a cause which at best can only be partly controlled. Thus far these lesions have been confined to the pons and have been relatively restricted in bulk. The chances are almost certain that similar accidents will recur. Either extensions to a medullary site or serious increase in the thrombotic areas produced can at any time inaugurate a fatal outcome.

CLINIC OF DR. GEORGE H. HYSLOP

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CONSTITUTIONAL INADEQUACY

Introduction.—As with physics and chemistry, the science of medicine progresses through development of knowledge of the common and concrete problems. Eventually one reaches the stage in which the phenomena under investigation at first glance appear intangible in their nature and which, although recognized as involving fundamental principles, nevertheless require a great deal of abstract thought in an endeavor to understand them. It is true, of course, that as one's knowledge of any given group of phenomena increases the seeming intangibility is found to be really quite concrete.

In every branch of the art of medicine the practitioner finds a type of patient who, in his clinical picture, presents symptoms that are not essential concomitants of the disease condition for which he may seek relief. For example, a patient may have a sore throat and, in addition to this, may have excessive sweating and a sour stomach, and be upset emotionally. These latter symptoms will be found to occur in this patient in every ailment he may have. The treatment of such a case may not necessarily be altered by these superimposed phenomena, yet such a patient is distinctly different from the person who when he has a sore throat has nothing else in the way of symptoms. The general practitioner, who must not only be able to diagnose the disease, but who must be able to weigh the value of these "unessential" clinical phenomena, should especially appreciate the clinical importance of this type of patient. In the specialties one is very apt to center his attention on the disease for which a patient seeks relief and shut the eyes to other, and seemingly irrelevant, matters.

The older generation of physicians used to make a great deal of what they called diathesis. By diathesis one has in mind the predisposition to not only a particular disease, but to groups of diseases. With the increase of knowledge of the preclinical sciences—physiology, bacteriology, pharmacology, and pathology—it seems there has been a tendency to forget that there may, after all, be such a thing as diathesis, perhaps because it was impossible to make accurate qualitative and quantitative observations, and because concepts that are difficult to submit to measurement are apt to be disregarded.

At the present time there is a quite definite and well-established habit of referring the problem of the type of patient to which this paper refers to neuropsychiatrists for opinion and study. Whether neuropsychiatry, or the body of medicine in general, is responsible for this custom makes no difference. Neuropsychiatry, nevertheless, has attempted to clarify our knowledge of this particular clinical problem, and some progress has been made.

The type of patient included in this group is not easy to describe accurately, but as good a way as any to define a large part of this group is to include in it those people who have been diagnosed as hysteric, neurasthenic, psychasthenic, and all those who, not only by the laity but even by physicians in general, are dubbed "nervous." The diagnostic terms mentioned do not mean exactly the same thing to every physician, but from the practical standpoint the average physician has a fairly definite idea of what sort of patient belongs in this group. Chronic appendicitis, gastric neurosis, and intestinal auto-intoxication are diagnoses frequently made upon patients for whom too often nothing much can be done, perhaps because clinical knowledge is not as yet correlated with an understanding of pathologic physiology. A fairly large percentage of the so-called rheumatism appearing in the third and fourth decades, and of the non-infectious type, occurs in patients who are usually found to be emotionally a little different from the rest of us. Hay-fever and asthma patients and also sufferers from certain skin conditions, which have traditionally been regarded

as due to some assimilative malfunction, comprise a group that, while not at all regarded as a problem for the neuropsychiatrist, yet, as time goes on, is gradually being recognized as having close kinship to the patients who in the past were referred to the neuropsychiatrist.

The reader may begin to think that I am trying to enlarge indefinitely the scope of neuropsychiatry and make a plea for considering all such patients as subject for investigation by neuropsychiatry. Such is not my idea at all, but for the sake of defining a problem which is really of clinical importance I wish to show that the problem applies to a large number of the sick. The family physician must be prepared to handle the majority of such patients, and his success will be proportionate to his understanding of them.

In association with these conditions which are dominated by physical symptoms one may also include the type of patient whose presenting symptoms are in the mental and emotional field—and are what might be called true psychoneurotics. This last mentioned clinical group has properly become the study of psychiatrists, yet I think that many of us realize that it is dangerous to have too highly specialized a division of labor, and that we have reached a point where further progress depends upon correlating the observations of different branches of the art and science of medicine as it concerns itself with the clinical groups herein mentioned. Neurologists are, by their interest, apt to emphasize the physical aspects of their clinical problems, whereas among psychiatrists there is a tendency to concentrate upon the mental or psychogenic features. In medical literature one finds that really the same clinical material may be studied from quite diverse viewpoints, and that, therefore, the conclusions reached by a given investigator are not broad enough, and in this way err from the truth. There is too much tendency to emphasize the symptoms which are regarded as predominant because they are of interest to the particular investigator. Possibly it is because of this that we find a conflict in the classification given a type of patient by different writers, and like-

wise it is for this reason that one fails to relieve patients of their complaints.

It is of interest to observe that it is not only the various branches of medical knowledge that contribute to our understanding of these patients. Sociology, eugenics, economics, and even anthropology find that really the same type of human being enters into their problems in an important way.

Perhaps it is time to coin a term which will be broad enough to refer to the human material the subject of this paper. In psychiatry we already have a term which at present applies to a fraction of this clinical group—"constitutional psychopathic inferiority." I think there will be no contradiction to the statement that there is also what might be called constitutional physical inferiority. I would like, therefore, to use the term "constitutional inadequacy" as applicable to all of the types of clinical conditions mentioned in this paper. It is true that this term does not refer at the present time to a clearly defined concept, but it may be an acceptable working term, and when our knowledge is better developed we may be able to devise a better terminology.

Constitutional inadequacy may be defined as a state of bodily and mental make-up which handicaps the individual in his adjustment to the various environmental stresses. The greater the degree of inadequacy, the more readily the individual presents evidence of what might be called decompensation. Some people are almost continually in trouble of one sort or another, while others may break only under relatively great stress. The degree of intellectual development does not enter into the subject discussed in this paper. It is true that genius, and especially those people who are talented in the arts, may show evidences of constitutional inadequacy. If such individuals become medical problems, they become so in spite of their intellectual qualities. Individuals with constitutional inadequacy might be referred to as human beings made out of "spare parts" which have been poorly assembled, without regard to whether the spare parts fit each other or not. Hence, constitutionally inadequate individuals go clanking through life very

much like the poorly assembled automobile which rattles its way down the street.

CASE REPORTS

A few cases, summarized briefly, will illustrate some of the points I have touched upon:

- I. Cases in which psychic stress was causal.
- II. Cases in which physical stress was causal.
- III. Cases in which no known cause could be discovered.

These cases, I think, demonstrate clearly that not only precipitating causes and symptoms, but the underlying constitution must be considered before one can reach a correct clinical estimate of his patient.

I. CASES IN WHICH PSYCHIC STRESS WAS CAUSAL

1. R. N. was forty when he enlisted. He was a bookkeeper and had never been seriously ill. He was closely attached to his mother and had never had any desire to marry. He was a passive type of sexual pervert. Physically he had female secondary sexual characteristics. While overseas he had difficulties with his commanding officer, who detected the perversion, and by his treatment of the man made him fearfully ashamed of his infirmity. During 1919, 1920, and 1921 the patient was so disturbed mentally that he had to be confined. Once he attempted suicide. He came under my observation in 1922. At that time he was the picture of a severe psychoneurosis. He could not sleep; the slightest noise startled him; there was a constant tic in which the head was jerked backward. He was unable to calm himself sufficiently to read anything; he avoided his friends; could not meet strangers; and had all sorts of fears and self-accusatory ideas. Physical symptoms, which dated back to the commencement of his mental state, consisted of insomnia, profuse sweating, fatigability, sour stomach, belching, and an obstinate constipation. During six months of psychotherapy alone, which had as its object convincing the patient that his perversion was an infirmity rather than a disgrace, there was a steady improvement in attitude, the physical complaints diminished in proportion, and there was a gain of 10 pounds in weight. Every few weeks he is apt to feel down-hearted about himself, and the physical symptoms at once recur. A brief talk is usually sufficient to make life comfortable again for awhile.

2. J. M. served in the infantry overseas. Previous to enlistment he was a mechanic and led an entirely normal life. However, puberty was late, he was subject to asthma and had a weak digestion. The horrors of front line duty affected him strongly, and he began to write poetry of a sort—a thing quite foreign to his previous temperament, which was about what one would call "hard-boiled." He slept poorly because of nightmares, grew sensitive, so that he would cry easily, and finally had some quite unusual mental experi-

ences. In a veridical hallucination shortly after the Armistice he became paralyzed on the left side, and saw a young German officer run over and killed by an engine emerging from a tunnel. (In 1922 the patient's mother visited relatives in Germany and learned that a young cousin, who had been a sub-lieutenant in the German Army, was in East Prussia and shortly after the Armistice had his left arm and leg severed and was killed by an engine coming suddenly out of a tunnel.) The patient began to have episodes suggesting psychic equivalents of epilepsy, and these made him fear for his future mental health. He still was troubled with nightmares, but during the day would fall asleep over his tasks. Bitemporal headaches were frequent, and he found that meats and fatty foods would upset him. This patient's condition continued relatively unchanged until the middle of 1923. Then he was rehabilitated from the vocational training given him by the government. The spur of economic independence seemed to stimulate him and he has improved mentally. The headaches have gone and his digestion is no longer troublesome. Of interest, however, is the fact that he is still subject to experiences indicating the presence of what is called mediumistic ability.

3. H. L. had a "nervous breakdown" late in 1922. She was then twenty-eight years old and had been married six years. As a child she was reserved, headstrong, made few friends, was hypercritical, and during adolescence not only had much menstrual trouble, but seemed dissatisfied with everything about her. She flitted from one thing to another in a fruitless search for "something interesting and worth while." She got along better for a few years after her marriage. Her husband then developed somnambulism and would make sexual demands when in his somnambulistic states, which sometimes occurred during the day. This shocked her, and finally she became "sick." Complicating the mental state was a low-grade pelvic infection, the residuum of a third-degree tear following labor. Her mental state showed sudden and marked variations for over a year, and during this time she insisted that there must be some serious physical condition which remained undiscovered in spite of the examinations of numerous consultants. Correlated with the mental state were certain physical phenomena—spastic constipation, blood-pressure and pulse-rate which fluctuated violently upon slight exertion or change of posture, dryness of the skin of the extremities, burning pains in the feet and shins after standing or walking. (These became worse when she lay down after exercise, and were more troublesome in the forenoon.) There were frequent rosacea-like eruptions on the face, associated with greasiness of the skin over the face, and an intense itching and scaling of the skin over her neck. Every few days she would have an emotional explosion, in which she would accuse her immediate family of being indifferent, call for her lawyer to make a will, and refuse to eat. An intercurrent pyelitis made her mental condition much worse and reinforced her idea that she was misunderstood and that she was seriously ill with something.

Intensive re-educative measures met with strong resistance at first. After a rather straight talk one day she nearly turned the house upside down. Then she began to improve, and after several weeks of careful handling decided that she was well. She seems to have changed her personality. She exerts self-control, shows consideration for other people, does not make a

fuss over little annoyances, and as a result of some selected reading seems to be thinking out a sane philosophy of life.

The physical phenomena, while at times distinctly under the influence of emotion, were modified by diet and proper medication. With this particular patient atropin and thyroxin were very useful.

II. CASES IN WHICH PHYSICAL STRESS WAS CAUSAL

1. M. C., age twenty-two, reported complaining of being tired, nervous, and unable to concentrate. His sleep was poor, he perspired excessively and had belching and constipation. These symptoms had troubled him for a month. Before this time his physical health had been perfect. He had never sought the company of girls, denied sexual intercourse, was an incessant reader, had no interest in athletics, and admitted that other young men thought him "different." His physique was of the "status" type.

On first impression this patient seemed to be a psychoneurotic. He suggested that his troubles were due to overwork—that being a bookkeeper by day and a law student at night was too much for him. After further questioning, it seemed that his symptoms had some physical cause, because his reaction did not quite fit that of the true psychoneurotic.

Examination revealed a severe infestation by pediculi corporis. Before the patient was acquainted with his condition he was asked what it was that disturbed his sleep. He promptly said, "itching," and added that the itching and disturbed sleep were the first symptoms to appear.

Appropriate measures destroyed the parasites and relieved the whole train of symptoms in a week.

2. P. F., age forty-five, came to the clinic complaining of nervousness, disturbed sleep, fears, and inability to "carry on" with her work. She had lost weight, was constipated, had hot flashes, and perspired. Her condition was of four months' duration, and began with mild digestive disturbances. She was an actress, and her husband had died of paresis. She had always been "nervous," and her recent symptoms led her to fear that syphilis was their cause. Medical examination led to the diagnosis of hyperthyroidism. Serology was negative. Examination in the Neurologic Department yielded no evidence of neurosyphilis. With the story given by the patient it seemed reasonable to regard her as suffering from approaching menopause symptoms, upon which was superimposed a syphilophobia.

Further questioning, however, brought from the patient the statement that her condition began to improve about two weeks before she came to the clinic. The improvement followed two quassia enemas, which cured a pin-worm infection that had probably commenced four months before when she was visiting in the country with friends whose children were at that time suffering with pin-worms. In any event, she recalled that itching appeared shortly after her return to the city, and about a week after this her digestive disturbances developed. This patient rapidly returned to her normal state.

3. S. S., age twenty-eight, complained of being afraid to ride in the subway, or to drive a machine. He perspired excessively, was so easily fatigued that he could not work, had a severe indigestion with intolerance of

carbohydrates and fats, and there was constipation and flatus. His trouble began early in 1919, when, after several months of unusual physical work, he became irritable, slept poorly, lost his appetite, and dropped 20 pounds in weight. The phobias appeared in 1920, and were accompanied by emotional instability, a loss of ambition, and inability to do any sort of intellectual work. His domestic life was perfectly happy. Physically: A long slender trunk with moderate visceroptosis, hypotrichosis, low blood-pressure, cyanosis of the extremities, and a functional systolic heart murmur. A rest cure, with physiotherapy, cured the patient in six months. No psychotherapy at all was used, and the mental symptoms diminished as the physical condition improved.

4. G. A., a young attorney, had a fractured skull. His father became incapacitated a few weeks later, and so the son had to cut short his convalescence and resume work, not only his own but also some of the responsibility of his father's business. In a few months he broke down—he became forgetful, felt unable to make decisions, could not concentrate, and became irritable. Also he could not sleep and had frequent headaches. His physician advised psycho-analysis. The psycho-analyst, after a persistent effort, failed to elicit a history of sexual dissatisfaction or of perversion. But he insisted that the patient was unhappy with his wife, and prescribed a mistress. The patient took the advice as well meant, but had the sense to ask how he would gain "happiness" through such a means when he felt no desire whatever for a mistress. And furthermore, he wanted to know, wherein would be the gain, in view of the fact that he felt certain that he really did love his wife and daughter, had a standing in the community to maintain, and did not wish to expose himself to the loss of his professional reputation. He concluded that the "cure" would be worse than the "disease," and decided to take a thorough rest. In six months he was well, and has been well ever since.

5. C. R., age thirty-two, had always been physically well, but was not well adjusted mentally to his environment. He was a problem while he was in school, never kept a job long enough to be promoted, and could not "tie himself down to a trade." He drank to excess occasionally. After the Armistice his platoon hiked about 200 miles in fifteen days, the men carrying heavy packs. He developed indigestion, lost weight, and became fatigued on the slightest exertion. After about two weeks of these physical complaints he went A. W. O. L. and was arrested while drunk. He was placed in hospital, and for two months was troublesome. He would fight the orderlies, swore at the doctors, and damned everything in general. His physical state improved and his conduct disorders ceased. A year later, after his return to civil life, he overworked again, and had another episode in which conduct disorders were prominent. This cleared up, and until he had influenza in 1923 he had no trouble. The influenza was only a mild type, but for nearly three months after it he behaved in just the same way he had done during his two previous breaks in mental adjustment.

III. CASES WITHOUT KNOWN ENVIRONMENTAL CAUSES

1. A. C., a woman thirty-five years old, would be incapacitated for several weeks once or twice a year. She had always been bashful, quit school aged fourteen after completing the grammar grades, and was too "nervous" to engage in any occupation before her marriage. She read only the newspapers, had no interests of any sort, and was emotional. Her menses appeared when she was fifteen, and had always been irregular—sometimes skipping two or three months. During the menses she was compelled to stay in bed because of severe cramps, flushing, and weakness. Her digestion was always poor and she could not do any heavy work because of fatigability. She professed to be happy in her married life, and had one child.

Her periods of decompensation were not associated with work, worry, infection, or menstrual periods. Their first manifestation was an irritability and excessive fatigue. Then headaches, poor appetite, loss of weight, "rheumatic pains," and constipation appeared. She would suffer in this way for from two weeks to two months, gradually recovering.

She was observed for a year, and during this time had two episodes of decompensation. At these times her blood-pressure was lower than usual, the pulse-rate stayed at about 110, 25 beats a minute more than her normal rate. Blood-count, blood chemistry, urinalysis, serology, and basal metabolism were all normal. Her complexion was muddy, the tongue was coated, there was a fine tremor of the fingers, and her tendon reflexes were exaggerated. Gastro-intestinal examination revealed nothing abnormal. There were no foci of infection.

Psychotherapy was of some help to her mental state, but, although numerous remedies were tried, nothing seemed to affect the somatic phenomena.

2. I. P., a woman forty-eight years old, had for two years complained of headaches, indigestion, a gain of 25 pounds in weight, soreness of the muscles and joints, and poor sleep. She was passing through the menopause, and presented also the mental phenomena usually associated with that epoch. Her physician had given her various "glands" without success. She stated that for years she had suffered much of the time from the same physical and mental symptoms. She knew of no cause for the onset twenty years previously, and careful questioning brought out nothing at all to account for the appearance of her trouble, except that during the preceding year she had gained considerable weight. With the onset of menopause the condition increased in severity. Examination revealed hypertrichosis which appeared in adolescence, and moderate obesity, nothing else abnormal. Laboratory tests were all negative.

3. H. L. was thirty-six years old, and sought relief from "nervousness." He had as a child been afraid of thunderstorms. During school life he was unable to hold his own with playmates—he was afraid of getting hurt, and had no aptitude for rough games. His classroom work was good, but he would stammer if the teacher seemed at all cross. Physically he was delicate, bruised easily, and his diet had to be watched carefully. He passed through adolescence without any untoward incident, but he devoted himself intensely

to his work because he "was good for nothing else." He married at twenty-four, and had 2 children. Domestic life was happy. From the time he was about eighteen years old he had migraine headaches, and frequent spells of indigestion lasting weeks at a time. On these occasions his personality defects were more troublesome, and he found it difficult to work efficiently because of insomnia, fatigability, and a heightened sensitivity, which expressed itself in fears and emotional instability to a point where he would cry if things went wrong. He had been psycho-analyzed without gaining any relief, and had tried to diversify his interests without success. The slightest untoward incident would bring on his symptoms.

Physical examination revealed hypotrichosis with feminine distribution of abdominal hair, hyperidrosis, dermatographia, and respiratory arrhythmia in a marked degree.

Pituitary diminished the headaches, diet and atropin controlled his indigestion and constipation, and although his personality defects persisted, he was much happier, with relief from his physical complaints, and eventually found an outlet in Boy Scout work.

DISCUSSION

Constitutional inadequacy may be either mental or physical in nature. From the psychologic standpoint the defect is usually in the field of emotion and volition. True intellectual deficiency of any appreciable degree brings into consideration other factors, and from the practical viewpoint might be excluded from this discussion. Physical inadequacy may express itself in certain abnormalities of structure or in faulty balance in the various endocrine and vegetative functions. The two are often correlated, but the latter may exist in individuals whose anatomic make-up cannot be with our present knowledge regarded as a real deviation from the normal.

Endocrinology, which has as its scope the study of the internal secreting glands and the vegetative nervous system, has attempted to group individuals into several distinct types. The literature of this branch of medicine offers perhaps the closest effort at a working conception of diathesis. Clinical anthropometry, a field of work in its infancy, is attempting to place on a more accurate and detailed basis the concepts advanced by endocrinology. It has already been suggested that there is a distinct correlation between certain anatomic characteristics and specific diseases.

The two types of constitutional inadequacy are by no means

to be separated from each other. On the contrary, it is common to find that individuals are defective in both physical and mental respects, although the inadequacy may manifest itself clinically in either a physical or mental way alone. The trend of medical literature during the last decade illustrates this point.

First, let us glance at the literature of psychiatry. Kempf has attempted to maintain that the personality of an individual finds correlated with it certain characteristic variations in the function of the vegetative nervous system. Further study of dementia præcox and manic-depressive insanity has contributed to our appreciation of the fact that these so-called constitutional psychoses frequently have constitutional physical deviations from the normal not only accompanying the actual psychoses, but often pre-existing. Children with the various conduct disorders must often be regarded as abnormal physically—not that their abnormal behavior is due solely to physical incapacities, such as deafness, poor vision, malnutrition, anemia, or the effects of faulty hygiene in general, but that there is an accompanying underlying defect in their physical constitution. De Sanctis recently, in a careful survey of a large number of such children, maintains that conduct disorders are, from the psychiatric standpoint, closely akin to manic-depressive insanity, and also that these children show physically distinct evidence of disturbed vegetative and endocrine function preceding and during the more marked periods of abnormal behavior.

Of course, these anatomic and physiologic abnormalities are not found in every psychopathic patient. The defects of function of the vegetative and endocrine systems may occur without the presence of gross anatomic variation from the normal, and in any event their presence must be determined and measured by the various laboratory methods. It is still necessary to maintain a perspective, and so far as we know now, although these physical abnormalities may occur among mentally normal individuals, they are more frequently found in psychopathic patients.

We find in certain types of neuroses a fairly high proportion

of these physical stigmata. Dysthyroidism, neurocirculatory asthenia, cardiac neuroses, and certain fatigue states may be mentioned as clinical conditions which are commonly associated with underlying constitutional physical defects.

Several infections may leave as sequelæ disturbances in both physical and mental fields. Such patients may be observed to have altered in temperament—unfortunately, as a rule, for the worse—or they may have for years gastro-intestinal malfunction, an exhaustible and unstable vasomotor system, a low threshold of resistance to infections, or an inability to stand physical strain of any sort. Painful feet, visceroptosis, and skeletal posture defects due to lax ligaments and poor muscle tone, may also be mentioned as some of the sequelæ. In examining a large group of such patients we find again that certain anatomic and physiologic types are much more frequent than in an equally large group of so-called normal people. In association with these various disorders of body function it is a rule to find that the patients are emotionally unstable, have a reduced capacity for intellectual effort, cannot stand responsibility, and, in general, are less able to maintain the mental level of activity which was their normal previous to whatever disease they suffered from. There is no general rule which enables one to give a prognosis. Each patient must be considered individually, and a great number of factors have to be weighed before one can reach a conclusion.

Chronic focal infection is particularly injurious to individuals who have either physical or mental constitutional inadequacy.

In the true psychoneuroses, in which not only the presenting symptoms but the causes of the conditions are in the mental field, it is necessary to determine whether or not in a patient there is also some form of constitutional physical inadequacy. Its presence, in my experience, exerts an important influence in the clinical picture, and is also a factor in the prognosis and treatment.

Returning for a moment to what may be considered as normal phenomena, in that they occur in everyone, we might mention the physical and mental instability associated with

adolescence and the climacterium. These periods of life are usually passed through with greater difficulty by individuals who show some form of constitutional inadequacy.

It might be wise to pause at this point and take stock. Psychiatrists are at times laughed at because they seem to think everybody must be regarded as abnormal merely because every individual has traits which theoretically would not be found in the perfectly sound human being. Even psychiatrists, strange as it may seem, realize that there is no such animal as the perfect man. A few abnormalities *per se* do not by their mere presence classify an individual as clinically abnormal or deficient. The mental and physical life-history of each individual must be studied as a whole before he can be judged as relatively sound or unsound. The enumeration of the clinical conditions above is merely illustrative, and I shall be content if it is understood that it is not the clinical picture alone that determines whether a patient is constitutionally inadequate, but rather the clinical picture plus his whole life-history. In other words, before one can classify a patient in the present, it is necessary to understand his past. This is a rather trite statement, but in spite of the tradition which has taught us to take family and past histories as a routine, I think it will nevertheless bear repetition and emphasis. It is necessary to elicit all sorts of information which the average patient will not yield unless his physician knows what questions to ask. If the physician is acquainted with some of the evidences of constitutional inadequacy he will understand his patient more intelligently.

What are some of the evidences of constitutional inadequacy? Again let us recall that they may be physical or psychic. The psychic defects may be classed as: (1) Disorders of conduct—vicious habits, criminal tendencies, excessive alcoholism, drug addiction, disorderly conduct, and the hobo tendency; (2) defects of emotional control, such as abnormal shyness and seclusiveness, phobias, irritability, bad temper, and mood deviations; (3) mental (these are scarcely intellectual qualities, it must be admitted)—egotism, stubbornness, and destructiveness.

The physical manifestations are of two forms—anatomic and physiologic. Among anatomic abnormalities are the gross deviations of structure and proportion from what would be normal in view of the individual's race or parentage. Of greater clinical significance are certain "stigmata" (including the sort of things described by Lombroso), such as abnormal palate, irregular spacing and disproportionate shape and size of the teeth, abnormal trichosis, and secondary sexual characteristics of the opposite sex. The physiologic evidences are chiefly manifestations of faulty function in the vegetative nervous system and endocrines. Vasomotor instability and cardiac and gastrointestinal neuroses are the commonest forms of manifestation of a defective vegetative nervous system. Patients with these conditions were a decade ago classed as either vagotonic or sympatheticotonic, but more recent knowledge regards such individuals as having an unduly irritable vegetative nervous system, and that the symptoms are seldom indicative of pure vagotonia or sympatheticotonia. Endocrinopathies may be responsible for some of the anatomic abnormalities.

There are certain diseases which in themselves may be considered as evidence of a physiologic inadequacy. Migraine and the various conditions classed under epilepsy, or the convulsive state, may be mentioned.

An individual presenting marked evidences of all three chief forms of constitutional inadequacy would be a pretty hopeless person. Such individuals exist and are usually more than a medical problem because their failure to handle environmental stresses usually calls for the help of sociology in solving their difficulties. The majority of constitutionally inadequate individuals do have defects in anatomic, physiologic, and mental fields, although the preponderance of deficiency is usually in only one field. The physiologic and mental defects are the more important clinically. Constitutional inadequacy is usually upon a congenital basis. However, it may be acquired, and in such cases manifests itself chiefly in the physiologic form, although if there is an endocrinopathy certain anatomic deviations may develop.

Again, it may be stated that the presence of constitutional inadequacy indicates a relative inability to stand environmental stress. Individuals with a slight degree of constitutional inadequacy may never "decompensate." Individuals with even several evidences of inadequacy may be efficient members of society unless circumstances conspire to make manifest their latent weakness. Individuals with high intellectual qualities may be handicapped by a poorly functioning body or by a faulty emotional make-up, yet they may still be valuable citizens. There are certain rather prominent politicians who unquestionably show the mental stigmata of constitutional inadequacy, and some of these, from information upon which one may place reliance, are also physiologically inadequate.

When constitutional inadequacy becomes a clinical problem, it must be kept in mind that not only the individual's defects, but the precipitating causes may determine the resultant clinical form manifested. However, experience shows that in a given individual the same clinical picture may be present at different times under quite diverse precipitating causes. Furthermore, there are some people who show what might be called a reversible reaction. Emotional stresses may produce in them physical symptoms only; yet on other occasions physical stresses will, in these people, produce an almost purely mental clinical picture.

The question of psychophysical parallelism can only be mentioned in this paper. Constitutionally inadequate individuals present a great many clinical phenomena which are relevant to that most interesting problem. The ultra-Freudians also have something to learn from this type of patient. To my mind the average psycho-analyst convicts himself not only of ignorance of physiology but also of an exceedingly lopsided and inadequate psychology. It is perhaps unfair to myself, as well as to psycho-analysts, to dismiss Freud and his disciples in a single sentence, but it is difficult to resist the temptation to criticize, because so many individuals with the various forms of constitutional inadequacy have been played with by psycho-analysts with conspicuous lack of success.

How shall such patients be treated? That question has a

complicated answer. Each patient is an individual problem. The therapeutic task is often quite difficult. Unfortunately, with many patients one is apt to be discourgaed at the prospects of relief, and is tempted to prescribe a tonic or a sedative, depending upon the most prominent symptoms, and let God do the rest. Sometimes this way is as effective as any. Seriously, one has to have available nearly the whole therapeutic armamentarium. Every measure—psychotherapy, through hygienic régime, drugs, and physiotherapy, down to skilful neglect—may be indicated. If the physician allows himself to rely upon a single form of therapy for all such cases he will relieve only the patients in whom that particular treatment is the chief need. His failures will join the throng who roam from one doctor to another and, unless in the meantime nature unaided performs the cure, many will become clients of the quack.

We have much to learn before constitutional inadequacy is a well-defined clinical concept, and its various manifestations understood in all their relations. As was suggested earlier in this paper, the first step is to correlate data from the various branches of medical science, not forgetting to draw upon any accepted facts that may be relevant in any branch of knowledge.

CLINIC OF DR. LEWIS STEVENSON

BELLEVUE HOSPITAL

THREE CASES OF SPINAL CORD TUMOR

THREE cases of spinal cord tumor are briefly presented here not because they have any particular interest for the neurologist, but because they are fairly representative examples of a not uncommon disease apt to be met with by anyone practising medicine.

The first of these cases went undiagnosed for at least six years after symptoms presented themselves. For three years prior to admission to hospital the patient had been practically helpless, and his tumor, as operation disclosed, had been growing in the meantime so that practically no spinal cord was left at the site of pressure.

The second case came to operation about one year after symptoms of spinal cord disease appeared and, during this period, the patient had been told, first, that her trouble was due to floating kidney; and second, she had been subjected to a laparotomy because of cramp-like pains in the abdomen which were later shown to be due to involvement of the ninth posterior thoracic nerve root, embedded in the cord tumor.

The third case came under observation not more than six months after any sign of illness was manifest and, although in this case the tumor was a psammoma and more easily removable than the other two, it still illustrates the great advantage of an early recognition of tumor in the spinal cord, for this patient recovered and the other two died.

In none of the cases was the diagnosis complicated by syphilis or any evidence of vertebral disease. There was no history of antecedent trauma in any of the cases, nor was there

evidence of neoplastic disease elsewhere in the body. The tumors were all primary growths of the spinal cord.

OUTLINE OF CASES

Case I.—A. M., aged thirty-seven. Hungarian male.

Chief Complaints.—Weakness of legs and arms. Numbness of legs. Sphincter disturbance.

Family history negative.

A.M.

Case ①

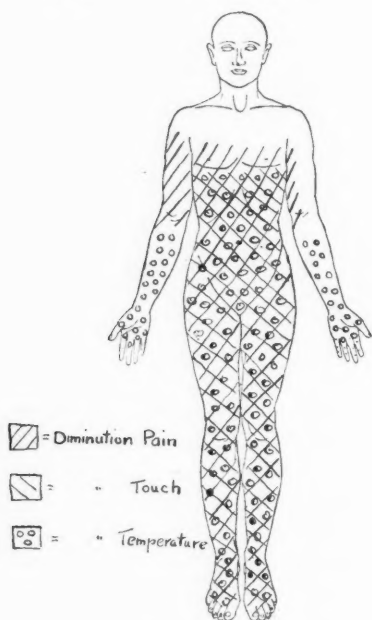


Fig. 102.

Past history negative except for diplopia five years ago; constipation since onset of present illness. Urgency and incontinence of urine for past four years. Worked hard as a farmer until three years ago. Some loss of weight.

Present Illness.—Onset six years ago, with numbness and weakness of both feet (felt as if he were walking on a mattress). Weakness and numbness of feet gradually worked upward, and four years ago had reached the hips, after which urgency and incontinence of urine and feces were noticed.

Three years ago patient lost the power in his legs and became unable to walk except at times. He became impotent and suffered from pains throughout the body.

Neurologic Examination on Admission

Cranial nerves normal except for some possible weakness of the eleventh nerve.

Motor Status.—Weakness of both arms with marked fibrillary twitchings of muscles. Spastic paralysis of both legs, with inability to walk. Some atrophy of both legs.

Reflexes.—Deep reflexes in arms diminished. Knee-jerks and ankle-jerks active. Double Babinski sign present. Abdominal and cremasteric reflexes absent. Marked defense reflex in legs.

Sensory Status.—Complete loss of touch and diminished pain below the level of D-4. Loss of temperature sense below D-5. Diminished temperature and pain sense over both lower arms. Loss of vibration and postural sense over both legs, with sensory ataxia of the legs. No tenderness on percussion of spine.

Operation (Dr. Joseph King, January 15, 1924).—Laminectomy C-5, 6, 7, D-1, 2.

Tumor found within substance of cord (submerged in it). Cord almost obliterated by growth and pressure of tumor, which measured $8\frac{1}{2}$ cm. long by $1\frac{1}{2}$ cm. wide. Site of tumor: Involved the cord from C-7 to D-3 segments. Slight xanthochromia or yellowing of spinal fluid. The tumor was found on examination to be a typical neuroblastoma.

The patient died on January 27, 1924, twelve days after operation.

Case II.—E. C., aged fifty-nine. Irish female.

Chief Complaints.—Both legs numb from hips down.

Past history negative except for laparotomy one year ago; loss of 60 pounds in weight in past year.

Present Illness.—Onset one year ago, with stiffness and soreness of right lower ribs and right groin. Two months later cramp-like pains in same region. Four months ago onset of numbness in hip region, which gradually crept down over legs. Now the legs feel cold and weak and the patient cannot walk; cramps in stomach continue; some urgency and polyuria, but no actual incontinence.

Neurologic Examination on Admission

Cranial nerves normal.

Motor Status.—Weakness of both legs, flexors more involved than extensors, right leg weaker than left.

Reflexes.—Lower abdominal reflexes absent. Deep reflexes of legs very active. Double Babinski sign. Defense reflex marked.

Sensory Status.—Level of hypesthesia at L-1 for pain and temperature, decreasing distally. Diminution of postural and vibration sense in legs.

Operation (Dr. Joseph King, December 22, 1923).—Laminectomy D-7, 8, 9, 10, 11. Subdural, extramedullary tumor found in right, posterolateral

position. Tumor measured $2\frac{1}{2}$ by $1\frac{3}{16}$ cm. and involved the posterior root of the ninth dorsal nerve on the right side. Tumor was subarachnoid at the level of eleventh and twelfth dorsal segments of the cord. Cord showed mod.

E.C.

Case ②

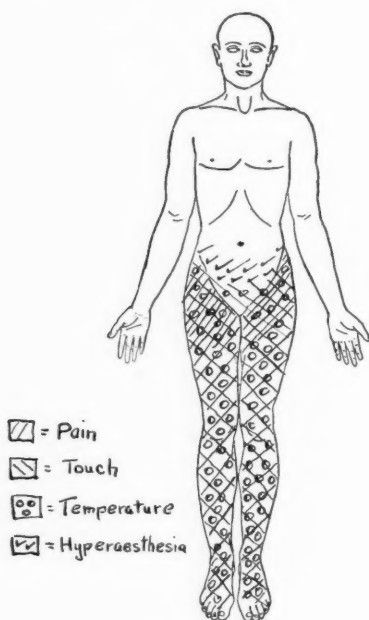


Fig. 103.

erate compression. There was no xanthochromia. Section of the tumor showed it to be a neuroblastoma.

The patient died on February 9, 1924, seven weeks after operation.

Case III.—O. T., aged thirty-four, American female.

Chief Complaints.—Unable to walk for past three weeks.

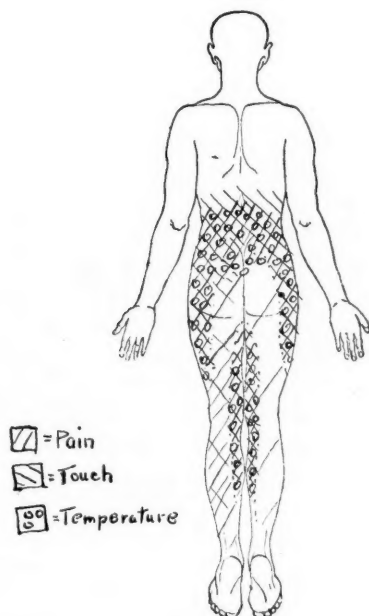
Past history negative.

Present Illness.—In October, 1922 legs gave way all at once while out walking; she fell down, but was able to continue walk, and felt well for next week. In November had several similar attacks, and felt some numbness through her right leg as she did at her first attack. In December she had an unsteady gait, and this grew steadily worse. Since January numbness felt from level of umbilicus downward over legs. She has also since this time felt

pain through her right leg, with stiffness at times. Since onset of her illness she has felt some pain around the waist which she ascribed to pressure of her corset. In past two weeks noticed delay in starting urine. Has had some burning pain in lumbar region since January. Weakness in legs progressively worse.

O.T.

Case ③



[Diagonal lines] = Pain
 [Solid black] = Touch
 [Grid of small circles] = Temperature

Fig. 104.

Neurologic Examination on Admission

Cranial nerves normal.

Motor Status.—Almost complete paralysis of both legs and lower part of trunk; no movement of legs.

Reflexes.—Arm reflexes normal. Knee-jerks and ankle-jerks very active; abdominal reflexes absent; double Babinski present.

Sensory Status.—Light touch absent below D-6. Pain absent below D-10. Position sense absent in toes and ankles.

Sensory Status (April 22, 1923).—Level of sensory loss D-8 with some questionable relative loss for a segment or two above this. Segments S-3, 4, 5, especially on right side, much less involved than segments above. No tender vertebræ.

Operation (Dr. Joseph King, May 12, 1923).—Laminectomy D-4, 5, 6, and 7. Extradural tumor found at level of seventh and eighth dorsal segments of the cord. It measured about $2\frac{1}{2}$ cm. long and lay dorsally over the dura, extending a little to the right side. It proved to be a psammoma on examination. There was no xanthochromia.

This patient, unlike the other two, did not die, but was able to go home on June 6, 1923, with a good deal of return of power in the legs and able to perceive pin prick in all the lumbar segments previously analgesic. Further recovery can now be confidently expected.

DISCUSSION

We have not given the histories or the neurologic examinations of these patients in detail. We have mentioned only the outstanding facts which should have led the physician to suspect the presence of spinal cord disease and, by an early diagnosis, not only to save the patient's life but also to give him a very good chance to recover power in his legs and enable him to resume his work. These three tumors were all benign and were all easily removed by Dr. King.

Numbness in the legs was a symptom in all of the cases. Numbness, in our experience, is usually the result of organic disease of the nervous system. Pain was also a symptom in all 3 cases. Persistent pain in the arms, trunk, or legs should at least arouse the suspicion of posterior root disease or actual involvement of the spinal cord. Persistent pain in an arm or leg is often the only symptom of spinal cord tumor for weeks or months before definite objective findings can be made out. The diagnosis of brachial neuritis or sciatic neuritis should not satisfy us until we have made every effort from time to time to rule out more important trouble in the spinal cord. Progressive weakness of both legs was the symptom which most concerned our patients, for it led in each case to total inability to walk. The progressiveness of this sign naturally enough leads to the impression of an expanding lesion affecting the cord especially, since the x-ray pictures were all negative for pathology in the vertebræ. The serology and, indeed, the history in each case gave no hint of cerebrospinal lues. Xanthochromia was present in only one case, but in all there was a definite increase of globulin in the spinal fluid obtained by lumbar puncture. The absence

of cell increase in the spinal fluid was against the idea that a meningitis, syphilitic or otherwise, was responsible for the symptoms.

Some disturbance of the bladder control was present in all the cases.

In each case there was a very definite level in the body below which pin prick and other sensory stimuli were not perceived at all or, if at all, very much less acutely than over the upper, normal portion of the body. This level could easily enough have been discovered in the course of a careful physical examination. The very presence of such a level makes us think of cord tumor at once and, when we find, in addition, indisputable evidence of double pyramidal tract involvement in the bilateral Babinski sign we have our diagnosis almost made. Further confirmation of a cord lesion is to be found in the absence of position sense in the toes. This sign was present in all the cases and was due, no doubt, to the fact that, in each case, the tumor lay over the posterior aspect of the cord and caused pressure upon the columns of Goll and Burdach which convey the sense of position from the joints of the toes to the brain.

The cranial nerves and cerebral functions were in each case normal with one trivial exception, so that the lesion causing the disability must have been somewhere in the spinal cord.

Three charts are included in order to show the level below which sensation was altered in each case.

CLINIC OF DR. CHARLES A. CLINE

BELLEVUE HOSPITAL

CASE OF MULTIPLE NEURITIS, WITH KORSAKOFF SYNDROME, FOLLOWING HYPEREMESIS GRAVIDARUM

THE occurrence of multiple neuritis following exposure to various toxic substances, notably alcohol, lead, and arsenic, is rather frequent, and it is not uncommonly observed as a sequel of the more severe infectious diseases. The incidence, however, of this disease resulting from the toxemias of pregnancy is quite rare, and a search into the various texts of neurology, psychiatry, and obstetrics is rewarded only by scattered references. In a very extensive and detailed contribution to this subject by Von Hosslin¹ the following statements are made: "That there is a form of multiple neuritis which takes its origin in the toxemias of pregnancy, which is wholly independent of any infection; that this malady may have its onset either before or after delivery; that when recognized, therapeutic abortion should be resorted to; that the termination of pregnancy hastens recovery; that convalescence is protracted, it having been four years before the patellar reflexes returned in one case which came under his observation, and that isolated neuritides may occur in place of the disseminated type, their location being determined frequently by intercurrent circumstances, such as slight trauma and stretching of the nerve trunks during the violent physical activities incident to delivery, or as result of pressure of the fetal head in the mother's pelvis."

The coincidence of Korsakoff's psychosis in the neuritides is of considerable clinical interest. This syndrome, of which the salient features are, impairment of immediate memory, mild mental clouding, confusion, and fabrication, was first described in 1887 by Korsakoff, who found it to be a very frequent

complication or symptom of alcoholic multiple neuritis. Since the advent of the automobile and the more extensive use of coal-gas several cases of Korsakoff's psychosis have been reported as occurring in carbon monoxid neuritides. Of interest is the statement of Von Hosslin, who finds that the Korsakoff syndrome is reported as having been observed in the multiple neuritides following toxemias of pregnancy long before Korsakoff placed his syndrome before the scientific world, and, in addition, observes that, *pro rata*, the incidence of this psychosis following gestational toxemia is greater than in alcoholic neuritis.

Ely, in a more recent contribution, describes 4 cases of multiple neuritis following hyperemesis gravidarum, and in each patient a memory defect of Korsakoff type was observed.

Multiple neuritis is invariably produced by the diffusion of toxins, exogenous or endogenous, which saturate the exceedingly vulnerable nervous system. Those of the former type are due to the absorption of chemical poisons, and are much more commonly observed, due perhaps to the marked tendency of chronic alcoholics to frequent the hospitals. Endogenous poisons are often infectious in origin, and it is undoubtedly true that the incidence of multiple neuritis is proportionate either to the severity and length of the illness (typhoid, tuberculosis, and pneumonia) or to the tendency of the disease to produce tenacious and virulent toxins (diphtheria and tetanus). The consideration of the poisons produced by metabolic disturbances leads us upon rather unsteady ground, and although the toxicology of gout and diabetes is more completely understood, the knowledge regarding the toxemias of pregnancy is still in a chaotic state. To quote Ely²: "At the present time we only know positively that certain toxins, apparently of endogenous origin, are frequently manufactured in the body of the pregnant woman, and do lead to eclampsia, pernicious vomiting, and other toxic phenomena. It is to be hoped that modern methods of research in the field of blood chemistry may clear up some of the theoretic speculation."

In discussing the pathologic anatomy of multiple neuritis the fact that the action of the toxins is not limited to the periph-

eral nerves is supported by the report of Stuart,³ who recites the autopsy observations made by him on a typical case following hyperemesis gravidarum. He found, on complete systematic microscopic examination of the central nervous system that, in addition to the classical changes in the nerve trunks, there were marked degenerative changes in the posterior and lateral tracts of the spinal cord, and also in the cells of the anterior horns.

This observation possibly explains the segmented muscular atrophy which has occasionally been reported.

Case Report.—Lillian L., aged twenty years; native of United States; housewife. Her family history was negative, and with the exception of measles in childhood and a subsequent tendency to nasopharyngeal infection, her previous health has been excellent. Previous to her marriage four years ago she attended night school and worked daily in an office. Her habits have been regular, and venereal infection is denied. Menstruation commenced at the age of fourteen years and, although the periods were very irregular, there was no excess hemorrhage or pain. Her last regular period occurred on January 20, 1923. The present illness began about March 20, 1923 with nausea and vomiting, at first infrequent and mild in character, but becoming progressively more severe and persistent and resisting all treatment. The patient was admitted to the Woman's Hospital on April 4, 1923 with a diagnosis of pernicious vomiting. Progress notes were as follows: Treatment: Dry diet, sedatives by rectum, and colonic irrigations. Vaginal examination: Signs of early pregnancy. April 10th: Vomiting at frequent intervals during day or night. April 15th: Vomitus included large quantity of fresh blood. April 18th: Bilateral parotitis observed. April 28th: Parotitis has subsided under local treatment, but the condition of the patient is much worse. May 10th: Cervix packed under gas-oxygen anesthesia (temperature 104° F., pulse 130). Patient aborted two days later. May 16th: Patient irrational (temperature 104° F., pulse 130). May 19th: Curetage of the uterus under gas-oxygen anesthesia, with removal of several fragments of normal placenta (temperature 101° F., pulse 100). May 22d: Patient incontinent and constantly irrational. May 31st: Temperature 99° F., pulse 85; patient complained of pain in the legs; Dr. Stevenson found patient with Korsakoff psychosis; pupils dilated and sluggish; retinal hemorrhage in right fundus; absent knee- and ankle-jerks; no sensory loss; wrist- and foot-drop. June 9th: Dr. Kennedy confirmed the diagnosis of polyneuritis with Korsakoff syndrome. During the next month, although the mental condition persisted, some improvement in the function of the arms was noted. A marked contracture, however, of both legs occurred, which involved both the hip- and knee-joints to a considerable extent. Laboratory reports for the preceding period included: Urine, specific gravity 1029 to 1032; faint trace to marked trace of albumin; occasional samples showed blood-cells and granular casts. On June 2d acetone and diacetic acid were present; urea 1.4 per cent. Blood:

April 16th; 5,120,000 R. B. C., 88 per cent. hemoglobin, and 11,450 W. B. C., with normal differential count. June 1st: 3,176,000 R. B. C., 70 per cent. hemoglobin, and 12,500 W. B. C. with slight polynucleosis; Blood Wassermann negative; blood urea 11.6 mg. On June 11th the patient was transferred to the Neurologic Institute. Here the Korsakoff psychosis gradually disappeared, and by August 15th the mental condition was fairly clear. The paretic condition of the arms almost completely cleared up, but continuous Buck's extension failed to straighten the contractures of the legs to any appreciable extent. The patient was admitted to Bellevue Hospital on October 27, 1923, and examination revealed the following: A fairly well-developed and nourished female, of flabby and anemic appearance; physical examination is negative except for these neurologic signs: Cranial nerves are negative except for inequality of pupils, the left being greater than the right. Motor: There is marked impairment of extension and weakness of the muscles of both upper and lower extremities. In the arms the extensors of the wrist are more markedly involved. There is considerable contracture of the hips and the knees, due to paralysis chiefly of the quadriceps extensor. The extensors of the feet are also weak, although there is beginning motility of the intrinsic muscles and the extensors and flexors of the feet. Sensory: There is reduction to all forms of sensation over the greater part of the lower extremities, more marked below the knees. There is loss of postural and vibration sensibility in the lower limbs. Reflexes: Abdominals are sluggish to absent; absent knee- and ankle-jerks on both sides. There is slight dimness of memory for recent events. After persistent extension of the legs with iron splints for three months, accompanied, of course, by massage and electrotherapy, the contractures were overcome. A residual fixation of the drop-feet by arthritic changes in the ankle-joints was treated by forcible extension, followed by the application of plaster casts. This condition was brought about by contracture of the Achilles tendon of both sides. At the present date the deep reflexes, sensation (superficial, postural, and vibratory), and considerable motor power have returned, although the patient is as yet unable to support her weight without assistance. There is still the slightest diminution of memory power.

CONCLUSIONS

- (1) That toxic multiple neuritis is a frequent sequel of hyperemesis gravidarum.
- (2) That therapeutic abortion is perhaps too long deferred in many cases of hyperemesis gravidarum, and is the best remedial measure and the most sure means of preventing multiple neuritis.
- (3) That a psychosis of the Korsakoff type is very prone to occur in this type of multiple neuritis.
- (4) That the prevention of contractures in the paralyzed limbs is an essential part of the treatment of this condition, and

that persistent forcible extension will suffice to overcome them should they occur.

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CLINIC OF DR. L. M. SHAPIRO

BELLEVUE HOSPITAL

SOME NEUROLOGIC SYMPTOMS CAUSED BY MALIGNANT TUMORS OF THE NASOPHARYNX. A CASE REPORT OF THE SYNDROME OF THE RETROPAROTID SPACE

ALL patients complaining of pain in the head, face and neck, and showing cranial nerve lesions should have the nose and throat examined and the glands of the neck carefully investigated. The close relationship of the nasopharynx to the second, third, and fourth nerves, the second and third divisions of the fifth and the sixth nerves; the gasserian ganglion; the ninth, tenth, and eleventh nerves; the last four cranial nerves and the cervical sympathetic nerve points to the importance of the necessity for such an examination.

New¹ reported 79 cases of malignant tumors of the nasopharynx within a period of six years, showing that they are much more common than we believe them to be. Woltman² also studied a large number of cases and pointed out the very small number of correct diagnoses when neurologic symptoms complicated the picture.

Most of the tumors occur in patients between the ages of thirty and sixty. However, they have also been reported in children under ten years. The symptoms may range from a few weeks to four years, the average duration being one year. The slow-growing tumors and those of a low grade of malignancy are the carcinomata of the mixed type, the clinically mixed tumors, and basal-cell epitheliomata. The lymphosarcomata grow very rapidly, and the fatal outcome occurs in from three to six months.

In the nasopharyngeal syndrome the patient may have pain (constant or recurrent) over the cheek, mastoid process, eye, frontal and temporal region. With gasserian ganglion involvement the typical pain of trigeminal neuralgia may appear and be followed by hypesthesia and anesthesia in the distribution of the fifth nerve. Many of the patients complain of ear symptoms—tinnitus, fulness, and gradually increasing deafness—and when nerve deafness can be eliminated the auditory symptoms are often found to be due to an extension of the growth into the eustachian tube. Many dramatic neurologic conditions arise when the plexus of cranial nerves at the base of the skull and below the parotid gland are caught. Six cases of nasopharyngeal and pharyngeal malignant tumors involving the cranial nerves in the region of the jugular foramen were recently reported by New.³

As to the latter, a number of syndromes have been described on the basis of certain definite symptoms added to a pure laryngeal hemiplegia. This is only limited by the possible combination of lesions—complete or incomplete—of the last four cranial nerves. The important thing to carry in mind is, *whichever other nerves are affected, the ninth, tenth, and eleventh are consistently injured together* by lesions in the region of the *jugular foramen*. The symptomatology of a combined ninth, tenth, and eleventh nerve lesion is rather constant and easily recognized, although some confusion still exists as to their separate functions. Vernet⁴ has pointed out a characteristic triad of symptoms indicative of a complete loss of function of these three nerves:

1. *Nasal regurgitation of fluids* due to paralysis of the palate.
2. *Dysphagia of solids* due to paralysis of the pharynx.
3. *Hoarseness* due to paralysis of the larynx.

Another favorite site in nasopharyngeal invasion is the retroparotid space. It is bounded posteriorly by the cervical spine, internally by the pharynx, anteriorly by the internal prolongation of the parotid gland, and above by the base of the skull in the region of the jugular foramen. The plexus of the last four cranial nerves and the cervical sympathetic nerve are here in close approximation, and a complete lesion of these nerves

is known as the *syndrome of the retroparotid space*. In substance the addition of the above symptoms (syndrome of Vernet) to the following signs makes the diagnosis:

1. *Atrophy and weakness of the sternocleidomastoid and upper part of the trapezius* (spinal part of spinal accessory).
2. *Atrophy and fibrillation of one-half of the tongue* (hypoglossal).

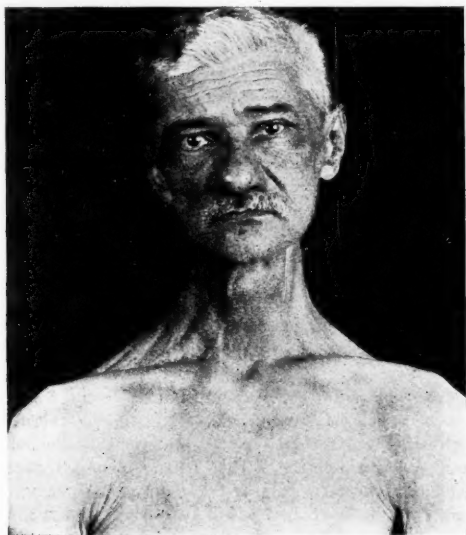


Fig. 105.—Cervical sympathetic syndrome on the left; pseudoptosis and enophthalmos; the myosis is not visible in the photograph. Also note the atrophy of the left sternocleidomastoid and trapezius.

3. *Cervical sympathetic syndrome of Horner*, the most important of which are:

- (a) Pseudoptosis, due to paralysis of involuntary part of levator palpebræ.
- (b) Enophthalmos, due to paralysis of muscle of Müller.
- (c) Myosis, due to paralysis of dilatator pupillæ.

From a review of the literature laryngeal paralysis associated with a syndrome due to paralysis of the last four cranial nerves

is not common, and is *usually due to a neoplasm*; less frequently, tuberculous glands and an acute phlegmon of the neck. During the World War cases were reported due to bullet and shrapnel wounds in this region; Pollack⁵ reported 3 cases. Stookey⁶ has reviewed the literature on multiple cranial nerve palsies with special reference to the retroparotid space, and the relation of the cervical sympathetic to the facial musculature.

Case Report of the Syndrome of the Retroparotid Space.—I. W., aged sixty-seven, cigar-maker, admitted to Neurologic Division, Bellevue Hospital, on February 25, 1924, complaining of left-sided headaches, dysphagia, hoarseness, tingling sensation of the tongue, marked weakness, and loss in weight.

Family history is negative.

Past History.—Patient has been an inveterate cigar smoker; and he has also complained of bilateral diminution in hearing dating back ten years before present illness.

Present Illness.—In 1917 patient felt a lump on the left side of his throat not associated with pain or difficulty in swallowing. It was removed at the Ear and Eye Hospital. The pathologic report was "infiltrating epidermoid carcinoma of the left tonsil." For two years he seemed to be perfectly well. The lump reappeared at the original site about January, 1920, and, on admission to the General Memorial Hospital, radium was applied. A satisfactory regression of the lesion was noted. Six months later patient was admitted to Montefiore Hospital complaining of pain on the left side of the angle of the jaw, slight difficulty in swallowing, increased salivation, and progressive loss in weight and weakness. The glands of the neck were enlarged on both sides and repeated block dissections of the left and right cervical lymph-glands were done. The patient remained practically free from symptoms until the early part of 1923, more than two years after the neck operations. Again he complained of pain over the left lower jaw and of increased salivation. In addition, there were dull, intermittent headaches over the left parietal and occipital region, which soon became excruciating and constant. A Roentgen examination of the skull revealed a small area of absorption of the bone. Radium, applied over this area, greatly relieved the pain. In June, 1923 entirely new symptoms appeared, and in such rapid order that the chronologic sequence is not definite. At first the patient experienced great difficulty in swallowing solids; the bolus of food appeared to be caught at about the level of the sternoclavicular joint and had to be washed down with water. Then the following train of symptoms appeared at one time: Hoarseness, tingling sensation of the tongue, impairment of taste, and dropping of the left lid. There were no visual disturbances, vomiting, or other evidences of increased intracranial pressure. The function of the palate was unimpaired apparently, for there was no nasal regurgitation of fluids.

The patient now enters Bellevue Hospital with practically the same complaints as those of a year ago, but he is unable to swallow solid food. Even

liquids tend to pass into the larynx, giving rise to coughing spells for some time after the foreign material has passed into the larynx. The deep Roentgen therapy is being continued, for it is the only agent that can relieve those excruciating headaches which now have spread over the entire left half of the head and face.

Physical Examination.—Patient is a cachectic-looking male of sixty-seven, who is constantly complaining of left-sided headaches. His voice is hoarse and rasping in quality. He co-operates well. There are no mental disturbances.

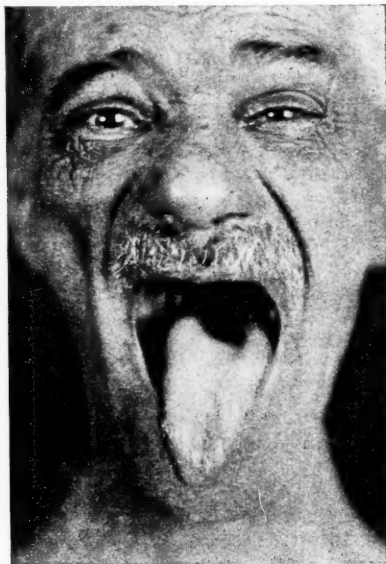


Fig. 106.—In addition to the left pseudoptosis and left enophthalmos note the marked atrophy of the left side of the tongue.

The fundi are negative. Visual acuity is good and there is no limitation of the visual fields. The extra-ocular movements are well performed in all directions; there is no nystagmus. The left pupil is smaller than the right, but both react well to light and accommodation. The left palpebral fissure is narrowed, with enophthalmos of the eyeball (Figs. 105, 106). The motor and sensory components of the fifth nerve are unimpaired; there is no corneal hypesthesia. The muscles of expression show no weakness.

There is no evidence of nerve deafness on either side, although hearing is bilaterally diminished. The palate reflex is equally present, but the left pharyngeal reflex is absent. Taste is absent over the posterior part of the tongue on the left. There is atrophy and weakness of the sternocleidomastoid

and the upper part of the trapezius on the left (Fig. 105). Atrophy and fibrillation of the left side of the tongue is present and is quite marked (Fig. 106). Laryngologic examination: Left side shows paralysis of the arytenoids and the vocal cords (cadaveric position); the epiglottis is deviated to the right.

Motor power is good at all the joints, and all the deep reflexes are lively and equal on both sides. There are no pathologic reflexes; the Babinski sign and other abnormal reflexes are absent. There is neither ataxia nor cerebellar signs. There are no sensory changes. There is no evidence of a lower motor neuron lesion.

The examination of the nose is negative except for slight deviation of the septum. No masses can be seen in the throat. The left tonsil is absent. There is no general glandular enlargement, nor can any glands be palpated in the neck. The examination of the heart, lungs, and abdomen is essentially negative.

The blood and spinal Wassermann reactions are negative. There is a marked secondary anemia with a color index of minus one. x-Ray of the chest is negative. The blood-pressure is 150/96. Urine analysis is negative.

I wish to express my thanks to Dr. E. P. Boas, Medical Director of Montefiore Hospital, for permission to examine the record of this patient.

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